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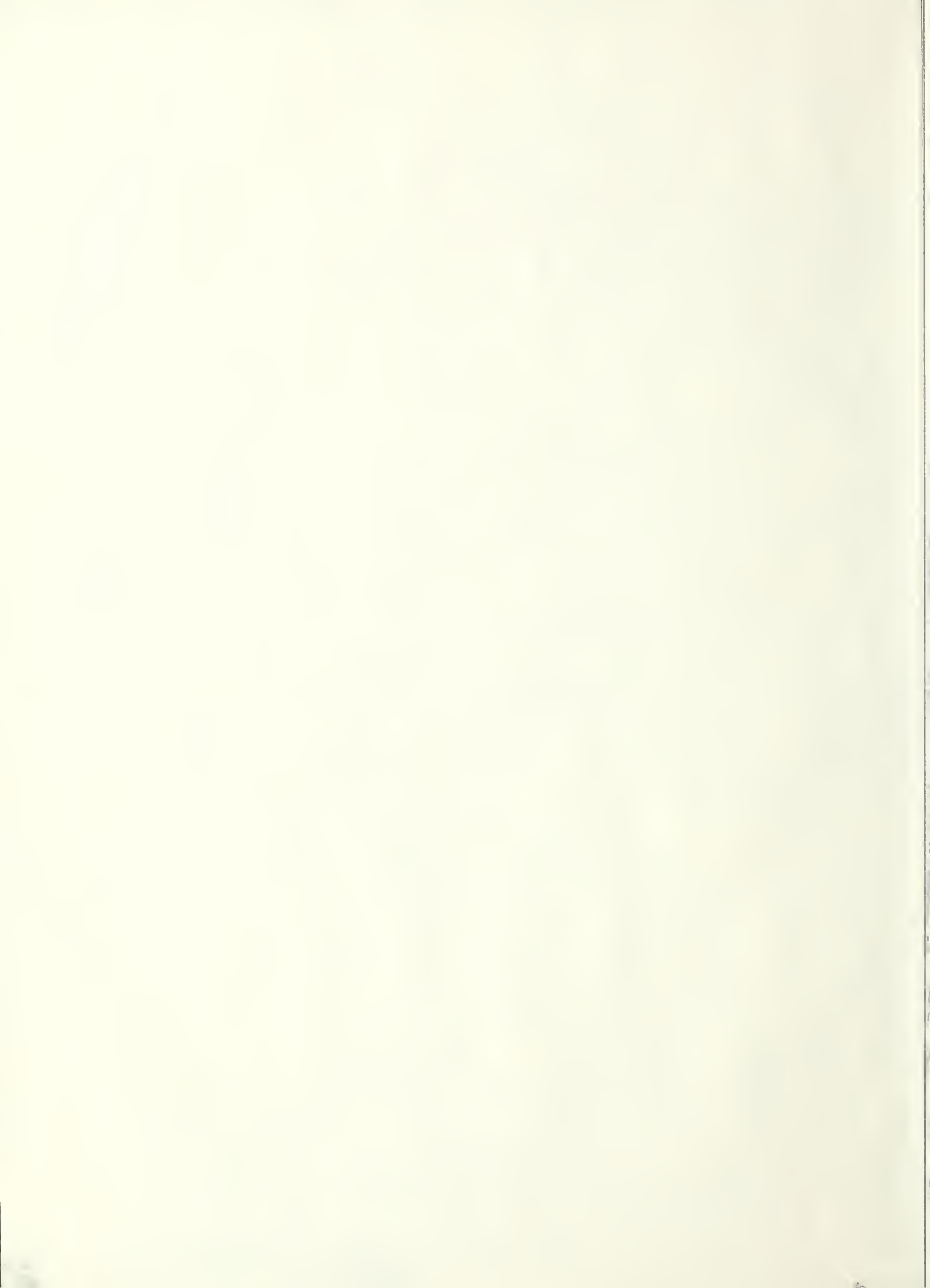
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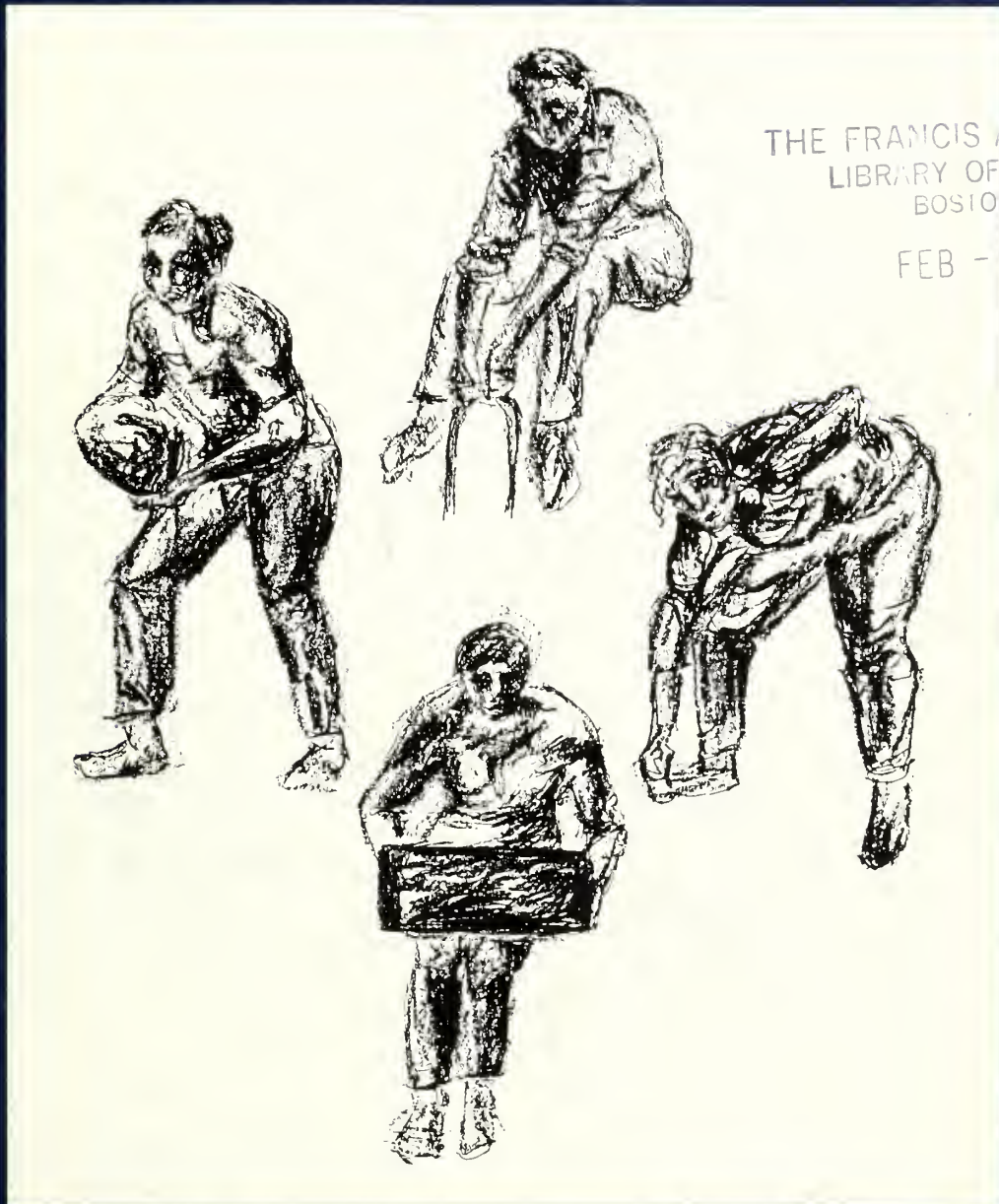
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January 1990

Volume 73, Number 1



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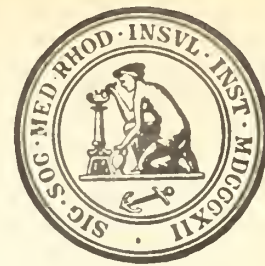
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Cover: Figure sketches depict common lifting, straining problems encountered at the workplace. Drawing by Jennifer Kennedy, a student at Rhode Island School of Design, Providence, Rhode Island.

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quirements. The company also sponsored regular educational demonstrations and programs. A year later the occupational injury/illness rates were redetermined. After the interventions, and with essentially the same workforce, significant musculoskeletal injuries (ie, those requiring one or more days away from the job) were decreased by about 80 per cent. The total injury rate dropped dramatically from 41.8 to 13.7 injuries per 100 fulltime workers per year. (Morb Mort Wkly Reps 38:413, 1989.)

Despite this example of improved working conditions achieved through employee education and ergonomic enterprise, the national occupational injury rates in manufacturing, construction and the trade sector have risen sharply in recent decades (Amer J Publ Health 78:276, 1988). Part of this rise in industrial morbidity may be the result of repetitive trauma disorders (eg, carpal tunnel syndrome). This form of cumulative injury accounted for 12.9 per cent of all work-related injuries a decade ago, but now is associated with 20 per cent of workers' compensation claims (Morb Mort Wkly Reps 36:713, 1987). Part of this rise, of course, may represent earlier underreporting but part may also reflect newer assembly line activities which require repetitive hand movements.

This issue of the *Journal* is devoted to a commentary on the phenomenon of cumulative trauma in the workplace, an ergonomic analysis of these chronic injuries, and a panel discussion of low back pain, a hazard which is certainly not confined to the workplace. Low back pain, indeed, is so commonplace that "my aching back" has become a metaphor for urban life, and, according to popular opinion, backache competes with the common

cold as the greatest challenge of biomedical research.

Stanley M. Aronson, MD

The Road from Troy

The practice of medicine relies increasingly on quantitative appraisals and guidelines. Repeatedly, we require to know: How much? How many? For how long? At what frequency? The good news is that of the many measureable physical phenomena (time, length, mass, capacity, force, acceleration, velocity) only a few are critically relevant to the daily business of medicine; the bad news is that many of us persist in using the colorful but archaic and illogical measuring units which had been devised for parochial needs centuries ago. We in the English-speaking nations still show a reluctance to adopt the metric system, a simple system which has been available to us for 190 years and which is the only standard of measurement observed in most countries of the world.

The bewilderments of the English systems of measurement are legendary. For the three major categories of quantitation (length, capacity and mass) we have willingly inherited a byzantine collection of historic residue which resist any facile attempts at interconversion. For ascertaining capacity, we have dry measures which include pints, quarts, pecks, and bushels; for liquid measures we are confronted with gills, pints, quarts and gallons; and for apothecary purposes, we are burdened with alchemy's minims, fluid drams, ounces and pints. For lengths we have inches, feet, cubits, and yards. Linear measurements in human medicine, fortunately, tend to be less

than a few yards and we therefore have no need in our descriptive clinical notes for fathoms (6 feet), rods (16 ½ feet), or furlongs (660 feet). And for mass, we are heir to three nonequivalent, vestigial systems: the avoirdupois system, involving grains, drams, ounces and pounds; the Troy system, using grains, carats, pennyweights, ounces and pounds; and the apothecary system, employing grains, scruples and drams. The Troy pound, of course, is only $12\frac{1}{16}$ of the commercial pound, and to compound the confusion, the British gallon is somewhat more capacious than the US gallon. The American pharmaceutical industry and the American Medical Association have long adopted the metric system as the simplest, most reliable means of conveying clear information among scientists, pharmacists, practicing physicians and the enlightened patient population.

There is little of redeeming value to the older systems except for some lingering nostalgia and an intriguing etymology underlying the names of its units. These units developed separately, were ambiguously defined and were related to other units of measurement only when forced to by circumstance. For example, a grain as the smallest measure of English weight, is first recorded in the court records of King Athelstan of England some seven decades before the Norman invasion. By the 16th century, the grain is defined as follows, "... *the least portion of weight is commonly a Grayne, meaning a Grayne of corn or wheat, drie, and gathered out of the middle of the eare.*" The dram (or drachm in the older texts), equals 60 grains and was originally determined by the weight of the Greek coin, the drachma. The scruple, of medieval apothecary usage, composed of 20 grains, is a term derived from the Latin

Table 1 Converting Units of Measurement

British System:

Fluid Measures [apothecary]:

1 pint = 16 ounces = 128 drams = 7,680 minims

Fluid Measures:

1 gallon = 4 quarts = 8 pints = 32 gills

Dry Measures:

1 bushel = 4 pecks = 32 quarts = 64 pints

Avoidupois Weight:

1 pound = 16 ounces = 256 drams = 700 grains

Troy Weight:

1 pound = 12 ounces = 240 pennywgt. = 5,760 grains

Apothecary Weight:

1 pound = 12 ounces = 96 drams = 288 scruples = 5,760 grains

Metric System (selected units):

Measures of Length:

name	meters
kilometer	10^3
hectometer	10^2
meter	1
centimeter	10^{-2}
millimeter	10^{-3}
micrometer	10^{-6}
nanometer	10^{-9}

Measures of Capacity:

name	liters
hectoliter	10^2
liter	1
milliliter	10^{-3}
microliter	10^{-6}

Measures of Weight:

name	kilograms
kilogram	1
gram	10^{-3}
milligram	10^{-6}
microgram	10^{-9}

scrupulum, a small sharp stone. The word now has greater currency as an ethical attribute than as a measurement. The carat is a word which descends from the Arabic, *qirat*, the fruit of the carob tree. The term carat may represent a weight, equal to about four grains, or a measure of the purity of gold expressed as a fraction of 24. Thus if a piece of jewelry contains 14/24ths pure gold and the rest, alloy, it is designated as 14K.

The word, inch, and the word, ounce, of widely different contemporary meanings, are both derivatives of the same Latin term, *uncia*, meaning a twelfth part. The fact that there are 12 ounces to the Troy pound, rather than 16, is one of many inevitable confusions which arise when weights and measures evolve by happenstance rather than by rational planning. The *avoidupois* system (from the old French phrase *avoir de peis*, meaning goods of weight) represented a market place system of commercial weights dating to the middle ages.

The Troy system, probably originating in the twelfth century mercantile fairs in the French city of Troyes, is still used in weighing precious stones, precious metals and certain pharmaceuticals.

The Babel of measuring units becomes even more distressing when still further non-European systems for weights, lengths and capacities are employed. Seventeenth century French scientists particularly the astronomer Picard, observed that the absence of a simple, easily defined and standardized system of weights and measures represented a major impediment to international commerce as well as to the evolving sciences of the West. Accordingly, earnest recommendations were made to develop a system based upon three attributes: First, that the fundamental unit of length be defined in relation to some unchanging physical attribute of the globe, and that measurements of capacity be a dependent function of this unit of length; second, that the basic unit of mass represent

the weight of distilled water, at a specified temperature, which is contained within a unit of capacity determined by the previously defined fundamental unit of length; and third, that all subsequent units of length, area, volume and mass (as well as their relationships to each other) be expressed in multiples of ten. In 1790 the National Assembly of France appointed a committee to select the basic unit of length from amongst three candidate criteria: (1) the length of a pendulum beating one second at sea-level, latitude 45° (2) a stated fraction of the length of the equator; or (3) a stipulated fraction of the quadrant of the terrestrial meridian. The committee chose the third and elected to adopt one ten-millionth part of this quadrant, calling this unit, a *meter*. The meter, and the other lengths, areas, capacities and weights derived from the meter, were finally documented nine years later and adopted into French law on December 10, 1799. In 1875, the In-

ternational Bureau of Weights and Measures was established in Paris to make and provide prototypes of the meter and the kilogram for the various countries of the world.

The two major systems of measurement (the metric and the English), and their interconversion factors, are outlined in the accompanying table.

The *Rhode Island Medical Journal* will continue to "think metric" and will remind its contributors that in things scientific, only the metric system will be acceptable. In other areas, we will not tamper. It would be unseemly to read King Lear described as, "... Ay, every centimeter a king!"; or Robert Frost reflecting, "But I have promises to keep, and kilometers to go before I sleep."

Stanley M. Aronson, MD

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Cumulative Trauma Disorders of the Upper Extremities

Henry M. Litchman, MD

Upper extremity trauma is now second only to back injury in causing industrial disability.

Scope of the Problem

It has long been recognized that activities in the workplace may adversely affect health. In addition to acute trauma, we are now concerned with the more subtle injuries that occur over time. The National Institute for Occupational Safety and Health (NIOSH) estimates that more than five million Americans, four per cent of the work force, suffered from these cumulative workplace disorders in 1986. Soft tissue musculoskeletal disorders including upper extremity and back problems now account for about 30 per cent of all workmen's compensation claims and it is predicted that this figure will reach 50 per cent by the year 2000.

Knowledge of these cumulative traumas has long been addressed. Bernardino Ramazzini¹ more than 200 years ago recognized two types of occupational hazards. The first was exposure

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to hazardous materials and the second was what we now call cumulative trauma disorders. He perceptively recognized "certain violent and irregular motions and unnatural postures of the body, by reason of which the natural structure of the vital machine is so impaired that serious diseases gradually develop therefrom."

Whenever there appears to be an increased incidence of disease we ask two questions: Is it occurring more frequently, or is it being recognized more frequently? In cumulative trauma it is probably both. In industry today there is an increase in assembly-line activities, an increased tempo of production and an increase in the use of vibrating and air-powered tools. Other factors such as an aging workforce and a reduction in worker turnover contribute to a growing incidence of cumulative trauma. There is also an increasing awareness that the symptoms arising from these diseases often emerge only after the worker leaves the worksite. Nocturnal symptoms were not recognized as work-related (and more related to the aging process) until patterns of symptoms correlated with specific risk factors in the working environment.² Upper extremity trauma is now

second only to back injury in causing industrial disability. Accident or acute injury is not the cause in a majority of cases.³

What we are now addressing are the injuries resulting from small traumas accumulating over time. These problems are not limited to any specific industry or occupation but rather to a pattern of usage. The vital machine, the human body, has great recuperative powers to heal its injuries if given the opportunity for repair through rest. The pattern that we have come to recognize is that when forceful, highly repetitive activity is combined with awkward posture and insufficient rest, a worker is at risk for developing a cumulative trauma disorder.^{2,4}

Some employers doubt that they have a problem in this area.

ABBREVIATIONS USED:

NIOSH: National Institute of Occupational Safety and Health

PRFF: Posture, Rate of contraction, Fatigue, Friction

SENSOR: Sentinel Event Notification System for Occupational Risks

SWET: Stress, Work, Environment, Tool-design

Some have used differing criteria in making this assessment. There may be a reporting of increasing occurrence, or they may have calculated the incidence or even analyzed the direct medical costs, payments to hospitals, physicians and therapists or the indirect disability costs — payments to the worker for lost time, lost productivity and disability settlements.

The incidence rate of a disorder represents the number of new cases occurring during a specified period of time for a given population at risk for the disorder. The period of time is measured in calendar time, usually a year. One must also know the exposure hours to a job. This calculation is usually made by estimating that each worker works 2000 hours per year (8 hours a day, 5 days a week for 50 weeks a year).

Using the formula:

$$\text{Incidence rate per 100 workers} = \frac{\text{No Cases/Yr} \times 200,000 \text{ wk hrs}}{\text{No Workers in dept} \times 2000 \text{ hrs}}$$

we can arrive at a figure which allows us to compare jobs, departments year-to-year comparisons as well as an industry-wide position.

As a guideline, a plant-wide rate of six cases per 200,000 work hours has been used as an acceptable base-line rate of injury. If one finds a significant variance in case rates between different jobs or departments one is on the road to identifying a problem. The next step is finding a solution.

We have already seen that there is a pattern to the process of developing a cumulative trauma disorder. The elements in this pattern can be thought of as risk factors that exist in the job itself and those involving the intrinsic capabilities of the worker. Injury

occurs when work demands exceed the workers capacity to meet those demands.

... a plant-wide rate of six cases per 200,000 work hours has been used as an acceptable baseline rate of injury.

We must therefore be knowledgeable in both areas and this is what is known as ergonomics or human factors engineering.⁵ To reduce injury we must analyze and adapt the man-made world to the human. This allows the workplace to be more efficient, safe and personally satisfying. It implies an interdisciplinary approach combining information on human characteristics as they define appropriate design of the job and its tools. Analysis of these risk factors is a good place to start as we may be able to identify sources of cumulative trauma before they become part of industrial statistics.

Human Factors

Ergonomic job analysis is a science that helps to identify and classify risk factors in the workplace. The weakest link in this science has been the medical components. Since design has to be user-oriented, we need to know more about the functioning of the "vital machine," the human body.

When thinking about risk factors, I use a memory device. When a worker is asked about his job demands, and the risk factors are low, the response is usually "no sweat." With a little poetic license, think of minimizing the risk factors as a "SWET-PRFF" system. The extrinsic factors that modify human function are represented by the first word (SWET). Each letter represents a descriptive word. Stress refers to factors such as obstructions, vibrations, and

temperature extremes. Work station and Environmental analysis involves the design of the work space for safety, ease, and efficiency. By examining the work environment, we can determine if the space and mobility provided is adequate or whether it forces the worker to assume abnormal postures or force requirements. Tool design is examined to determine if the productivity benefit is not offset by the risk inherent in the use of the tool itself. We look specifically for high contact forces, static loading, abnormal postures and repetitive motions.

The second word in the memory device — PRFF — refers to the human factors. They cannot really be separated from the engineering factors but must be looked at from the physiological viewpoint. The activity which the human body contributes to the industrial equation is muscular effort. We think of the hand as the end organ (tool) with the rest of the upper extremity being a positioning and motor device. We usually describe this mechanism in terms of strength. Strength is a term, however, that cannot be quantitated in measurable units. What we can measure is force, torque, work and power output.

There are two kinds of muscular effort. Static effort requires a prolonged state of contraction and dynamic effort is characterized by rhythmic contractions.⁵ Although most activities are a combination of the two, the body tries to conserve energy by minimizing static contractions since it is less efficient since with prolonged contraction, the blood supply is restricted and forces cannot be sustained.

We characterize the elements that contribute to what we call strength using our acronym PRFF. Posture is an important determinant. The amount of force that a muscle can generate is related to

the length of the muscle tendon unit at the time of contraction. This is shown in the length-tension curve which illustrates that there is an optimal length for maximum tension. The length is determined by the posture of the joint over which the tendon passes. As an example, the wrist in flexion functionally lengthens the tendons for grip. Grip strength is weaker and more force has to be generated to accomplish the task. Another instance where posture affects function is by determining which muscles will be used to carry out the task. For example, a task requiring force generation in supination utilizes the biceps muscle predominantly. Pronation force uses weaker muscles, fatigue more quickly and are prone to injury. One of the most common problems in industry is called lateral epicondylitis or tennis elbow and represents injury to the origin of the extensor muscles of the forearm from overuse of the muscles used in a pronated posture. In the hand, pinch grip (holding the object between the thumb and fingertip on the side of the index finger) allows only 20-25 percent of the force that can be generated when the hand encircles the object (power grip).⁶ This will also vary with grip span which is a third mechanism related to mechanical efficiency by virtue of posture. Since the biceps tendon attaches to the forearm at a distance from the axis of rotation of the elbow, the torque (force x distance) generated by the biceps muscle will be greater when the elbow is flexed at 90 degrees than when it is extended.

Rate of contraction is the second determinant of what we call strength. Activities that require a continuous contraction (static effort) are associated with decreased blood supply and buildup of toxic metabolic products and cannot be sustained. Most

activities are more dynamic and we refer to this as the rate of repetitiveness with which contractions have to be performed to do the task. This is usually measured in cycle time (the number of movements that occur in a given time in order to complete a given task.) We must also know how often the cycle time must be repeated. The more repetitive the task is, the more rapid and frequent are the muscle contractions. Higher velocity contractions develop less force than slower velocity contractions for the same load. Muscle effort if increased over prolonged periods of time can produce trauma even at what may be otherwise considered safe levels.

The third determinant of strength is the intrinsic Force that a person can ideally generate. Each muscle fiber contracts with a certain force and the strength of the whole muscle is the sum of the strength of its fibers. Since women in general have less muscle bulk they generate about 30 percent less force than a man, assuming equal conditioning.

The final determinant of strength is *Fatigue*, defined as a state of lessened efficiency and decreased effort. Not only is force reduced but movement is slower, coordination may be impaired and there is, in addition to decreased productivity, an increased risk of error and injury. It results from the buildup of metabolic waste products due to insufficient rest and metabolic recovery, a combination of the previous three factors. In terms of risk of exposure, think of taking a picture with a camera. The proper exposure is determined by (1) the lens opening, representing the intensity of light or forces, (2) the shutter speed, representing the duration of the light or forces and (3) the film type — representing intrinsic character-

istics of the film emulsion or the person's muscle. Different people will, by virtue of these intrinsic characteristics, function at different fractions of maximal capacity. When activity reaches 40 percent of maximal capacity, blood flow reduction to muscle is measureable, and at about 70 percent is significantly lowered. We should be aware of the factors that cause us to have to increase our intensity or duration of effort. A good example is the necessity to wear gloves. This is often necessary for mechanical or thermal protection. Grip strength is decreased proportional to the thickness of the glove, thus increasing the force requirement to accomplish the same task. Another modifier of force requirement is the surface Friction of the load to be handled. The force required to hold an object is proportional to the force causing it to slip out of the hand. It is inversely proportional to its slipperiness (coefficient of friction). A dry hand (CF = 0.5) is more slippery than a moist hand (CF = 2.0). The best example of this is turning a book page. It is rendered easier by moistening our fingers. Another example of increasing the required forces is in the use of tools that vibrate.⁷

To a great extent we can modify the workplace and control the factors of intensity and duration. It is often necessary, however, to be sure that we choose the right person for some jobs.

Strategies for the Control of Cumulative Trauma Disorders

In each situation one is always faced with the risk-benefit ratio, often an individual determination. We can think of heightened productivity as increasing gross revenue, but as work pace increases human cost and rejection rates of imperfect products may become significant.

We must first start with problem recognition. Recording the incidence rates of trauma may help to recognize the problem, but does not evaluate the causes.

Problem evaluation begins with better statistical evaluation, seeking common denominators. There are several methods of approach in evaluating the problem once it is defined. One method surveys health care providers to try to develop reliable data. This has not been too successful. Standard definitions are not always available, health professionals are not always adequately trained and usually only a small per cent respond to surveys (30 per cent in a recent study).⁸ There is an effort between NIOSH, the Center for Disease Control and ten state health departments to develop the Sentinel Event Notification System for Occupational Risk (SENSOR) program to improve occupational disease surveillance at state and local levels. They have, for example, recommended a definition for carpal tunnel syndrome.

Risk managers should look more carefully at medical reports to see if the care givers are providing objective findings to support their diagnoses and conclusions as to the ability to work. If there is evidence of work-related injury in the work environment, a job analysis is indicated. Worker assessments can be helpful but are difficult to evaluate. Based on this information, design modifications can be suggested, tested and evaluated. The object is to fit the job to the worker.

In some instances it may be more practical to fit the worker to the job. Pre-employment evaluations are not cost effective except in high risk jobs. When undertaken, the examiner must be provided with an accurate job description. The examiner must be able to evaluate the physical ca-

capacity of the worker and report the medical findings to employers in a form that helps them to make decisions. It should also provide a baseline for any future treatment or disability determination.

When functional capacity cannot meet the job demands, injury will inevitably result. How capable are we of determining functional capacity of the upper extremity? We have made great progress in determining trunk and leg dynamic function but as yet there are few standards for the upper extremity.⁵ There is no methodology to predict susceptibility to cumulative trauma disorder in the upper extremity. Wrist measurement ratios have been suggested but not confirmed for predicting carpal tunnel syndrome. Sex differences are not often significant.

If pre-employment screening is based on weak criteria it may be discriminatory either under federal law (Rehabilitation Act of 1973) or under the laws of some 44 states. We have to be able to show the relevance of a screening test. It must identify the minimal and essential attributes needed by a worker to satisfy and effectively perform the job. The screening must be performed dynamically so that it accurately simulates the job demands.

The significance of being able to test a person based on these criteria is far-reaching. When a person becomes injured we must determine the degree of functional impairment, the ability to return to work, what kind of work, and if unable to return, the degree of enduring disability.

For lifting tasks and grip-strength requirements, standardized, separate isometric measurement can be interpolated into valid measurements of function, assuming that the effort is maximal. Once a person is injured, de-

termining that the effort during testing is maximal becomes more difficult. There are no dynamic studies that can simulate the work place.

Another method for preventing cumulative trauma disorders has been job-training. The objective is to increase awareness by education and to change behaviors thus reducing risk factors. Industrial training programs are easy to implement and seem intuitively to be helpful but ultimate value is questionable. Training programs are not a substitute for ergonomic interventions. Training programs, however, heighten awareness of potential problems, the first step in problem solving. Also by establishing protocols, it makes it easier to integrate new employees into specific jobs.

Realizing that there are inevitable risk factors inherent in any job, another strategy minimizes them by reducing exposure. One consideration, for example, may be worker rotation. This is not without its own risks. Adjustment to different tasks is not always easy or productive. The ultimate goal is to reduce physical fatigue and stress. We don't know in most cases the end point when fatigue might pose a risk factor. Another area of consideration is in not providing incentives to pass up rest periods. Bonuses for productivity may result in increased injury rates and inferior products.

Even with all these strategies, we have to accept that a certain number of workers will become injured on the job. What further strategies are available to minimize the effects of these injuries to the worker and to the employer? It begins with the initial handling of the injury when first reported. Concern for the injured worker and directing him to quality care is the only chance for exerting any control during this phase of the problem. Failing this,

the worker will be lost in the care system and if there is fear of economic loss, may seek redress through legal help. The workmen's compensation system was designed to avoid litigation and the fact that there is so much, demonstrates a failure of the system.

More than five million Americans, four per cent of the workforce, suffered from these cumulative workplace disorders in 1986.

Physicians must ask how much do we contribute to this failure? If the primary medical report had documented a causal relationship, would this have facilitated earlier insurance payments? When the injured worker is sent for medical care, the employer expects prompt service, good liaison and immediate answers as to the status of that worker. Maintaining contact shows the injured person that the employer's concern is continuing. Reporting should be rapid and should contain quantitative data to substantiate the diagnosis and establish work capacity. The health care provider should be accountable not only to the injured worker but to the employer. This is not a conflict of interest. The interest of all parties should be the restoration of the employee's health and his return to normal activity in a rapid and effective manner.

The employer should try to keep the worker in the workplace. Most injured workers are not totally disabled and with the proper information from the health-care provider, suitable alternative employment may be provided. There are many reasons to support this recommendation. Too much rest leads to deconditioning and pro-

longed disability. The longer a worker is out, the harder and less likely will be his return to work. It is also in the best interests of the employer to continue rehabilitation until the worker returns to pre-injury function.

Prevention is better than cure. If and when injury occurs, however, the involved worker should be directed to a knowledgeable provider who believes in early and aggressive management. The care giver must be accountable to both the patient and the employer and provide documentation of an objective nature. In order to function well, the workmen's compensation system will require rapid resolution of questions that too often are delayed. Causal relationship, diagnosis, and work capacity should be documented. Prompt reporting and good communications are a key to the medical and financial health of the injured worker. Motivation is the most important element in a successful outcome and it requires considerate health givers as well as personal job satisfaction and employer support.

References

- ¹ Ramazzini, B., Wright, W. (Translation) The Diseases of Workers, University of Chicago Press, 1717 and 1940.
- ² Putz-Anderson V: Cumulative Trauma Disorders: A Manual for Musculo-Skeletal Diseases of the Upper Limbs. New York: Taylor & Francis, 1988.
- ³ Hadler, N.: Bailliere's Clinical Rheumatology, Vol. 3, Page 121, 1989.
- ⁴ Silverstein, BA: Fine, LJ, Armstrong, TJ: Hand Wrist Cumulative Trauma Disorders in Industry. Brit J Indust Med 43:779-784, 1986.
- ⁵ Grandjean, E., Fitting the Task to the Man, 4th Ed., Taylor & Francis, Philadelphia, 1988, pp. 24-25.

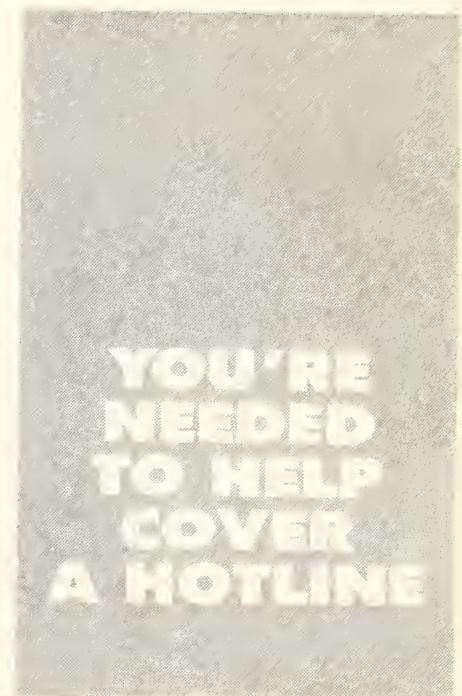
⁶ Armstrong, TJ: Ergonomics & Cumulative Trauma Disorders. Hand Clinics 2:553-565.

⁷ Radwin, RG; Armstrong, TJ; Chaffin, DB: Power Hand Tool Vibration Effects on Grip Exertions. Ergonomics 30:833-855, 1987.

⁸ Occupational Disease Surveillance, JAMA, Vol. 262, No. 7, p. 886, Aug. 18, 1989.

⁹ Snook, S. H., The Design of Manual Handling Tasks, Ergonomic, Vol. 21, No. 12, 963-985, 1987.

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Ergonomics: A Help in Understanding and Preventing Cumulative Trauma Disorders

Guy Fragala, PhD, CSP

Ergonomics . . . is defined as the scientific study of the relationship between human beings and their environment, particularly in the workplace.

Ergonomics, human factors engineering, can be helpful in improving the work environment. The term ergonomics, which originated in England, is defined as the scientific study of the relationship between human beings and their environment, particularly in the workplace. The field of ergonomics became a defined discipline during the rapid military build-up of World War II. Equipment became so complex and operating speed so high that workers were subjected to much stress, resulting in equipment or operational failure. It became necessary to learn more about the limitations of human performance and then to design operational systems that would accommodate these limitations. The basic goal of ergonomics in the workplace is to design operational systems to fit the worker rather than expect the worker to adapt to poor workplace design.

Figure 1a shows the location of controls for an industrial lathe in

relation to a typical worker's height. Many of the controls are below waist height and at more than arm's reach from the center of the workplace. Figure 1b depicts what a person would have to look like in order to possess the reach and visual control capabilities needed to comfortably operate this lathe.

One of the starting points when considering the task of designing equipment to fit the individual is to determine limitations of human strength and reach. Beyond just specifying the physical dimensions of work stations, ergonomics focuses on the total workplace, considering comfort and safety of the worker with respect to lighting, noise, heat and other environmental conditions. The design and placement of display panels and machine controls so that they do not overstress worker limitations, must also be considered. Simply put, ergonomics tries to make workers as comfortable and as safe as possible in the workplace so that they can perform optimally without being overstressed.

The principles of ergonomics are applied in an attempt to prevent some of the more serious musculoskeletal disorders en-

countered in industry today, such as back injuries and cumulative trauma disorders of the upper extremities. This article will focus on application of ergonomics as a preventive intervention aimed at reducing the impact of cumulative trauma disorders of the upper extremities in today's industrial environment.

When considering this grouping of occupational injuries we can consider a set of contributory risk factors:¹

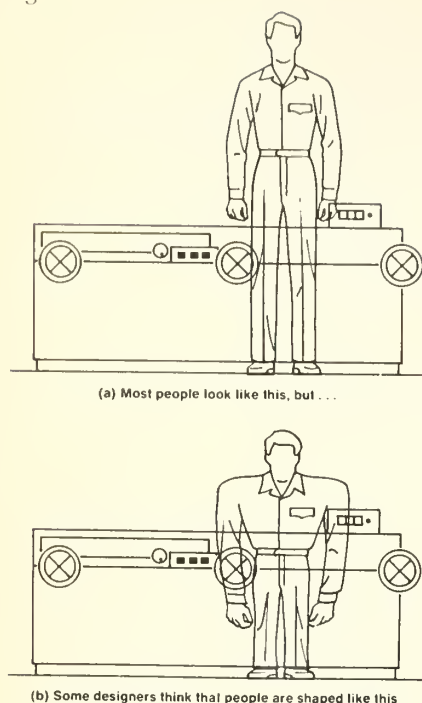
- (1) Work posture
- (2) Tool design
- (3) Mechanical stresses on body parts
- (4) Grip force required to accomplish the task
- (5) Repetition
- (6) Vibration

As the presence and intensity of each of the above risk factors increases, the likelihood of cumulative trauma disorder type injuries will increase.^{2, 3} Through ergonomics it may be possible to eliminate or reduce the intensity of one or more of the risk factors present.

Let us begin by looking at posture. The optimum position for the hand and wrist to assume when

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Figure 1.



doing work is the natural or neutral position which is the position of the wrist when the arm and hand hang by the side of the body. If a work task requires wrist flexion, extension, ulnar deviation or radial deviation, additional stress is placed on the worker's arm and hand. Through the application of the principles of ergonomics, job tasks which require bent wrist posture are observed and design changes considered which will accommodate the worker better. For example, a seated operator feeding components to a semi-automated machine may have to assume a posture with an elbow angle of about 50 degrees. As a result the worker's wrist may be in flexion and ulnar deviation. A simple adjustment of the seat allows the angle at the elbow to approach approximately 90 degrees. The 90 degree bend at the worker's elbow will allow the wrist to assume more neutral and comfortable posture to accomplish the job task.

Tool design can present another risk factor. A task using a

pair of pliers may require the worker to bend the wrist in palmar flexion or ulnar deviation or both. Figure 2 illustrates some poor occupational postures of the wrist due to the placement of the assembly and repair work and tool design. A simple modification to this task would be to obtain a new tool where a bend would be placed in a tool replacing the bend to the wrist. For example, rather than using conventional pliers, pliers could be obtained with a bend between the plier jaws and the handle of approximately 120 degrees. These ergonomically designed pliers are illustrated in Figure 3. The rate of tenosynovitis, epicondylitis and carpal tunnel syndrome is much greater for those workers who used conventional pliers, as opposed to bent pliers.⁴

Tool design can also contribute to the third risk factor, mechanical stress with tissue compression. The handle design of a hand-tool may dig into the palm and obstruct blood flow or the sharp edge of a work bench may compress the worker's forearm. Figure 4 illustrates how a short pair of wire clippers is used to perform a repair task. Although the pliers are small enough to get into restricted spaces they do not extend beyond the center of the palm. As force is applied it is transmitted to the base of the thumb where nerves and blood vessels pass through the palm. Repeated trauma to this part of the hand may produce soreness or damage. The impact of mechanical stress to the palmar surface can be reduced through better tool design. Consider a simple tool such as a screwdriver; if the length of the handle is too short it will push into the palmar surface of the worker's hand. A simple modification extends the length of the tool handle. The optimum length of a screwdriver

handle is approximately five inches. The same principle can be applied to the pair of pliers shown in Figure 4. Pliers with short handles causing palmar compression can be improved by padding and extending the handle length, as illustrated in Figure 3. Mechanical stressors caused by sharp or hard work surfaces can be minimized by simply padding the work surface.

Pliers with short handles causing palmar compression can be improved by padding and extending the handle length...

The fourth risk factor, required grip force, is significant in contributing to cumulative trauma disorders.⁵⁻⁸ If a worker must continuously use excessive force to complete a task, fatigue will soon result.



Figure 2. Poor occupational wrist postures with conventionally designed hand tools.



Figure 3. Ergonomically designed pliers; compare with figure 2.

One factor to consider with regard to grip force is handle span. Figure 5 illustrates average maximal grip forces in Newtons and pounds-force for women at several different grip spans. This illustration demonstrates the inefficiencies which develop when span is too small or too large. Designers should be aware of optimum grip spans when designing machine or process controls.

Redesign of the work station may be one answer to reduce required grip force or a closer look at the manufacturing process may reveal other interventions which can improve the situation. For example, if an assembly task requires pushing two components together the fabrication process prior to assembly may be set for a closer tolerance range which will then facilitate assembly. A lubricant may also be used to aid the assembly process.

Another reason for excessive force requirements may be that components of tools wear out. Preventive maintenance principles could be applied to replace tool components prior to worker complaints. Employees may also be trained in the application of

better methods to reduce the amount of grip force required to complete a task.

The fifth risk factor is repetition. The more times a motion is required in a fixed time period the more stressful it will be to the worker. Traditionally, work rates have been set for incentive systems in the manufacturing environment. When workers are observed by engineers to set work rates, consideration may not be given to the fact that a particular rate over number of weeks can

over-stress body components. There are many ways to reduce repetition. Some examples include: job rotation among workers in a particular department whereby workers are involved in varying tasks over the course of the workday; process design, so that an individual worker assumes more of the assembly tasks for a particular product thus reducing the repetition of the same action; and scheduling periodic work breaks.

... ergonomics tries to make workers as comfortable and as safe as possible in the workplace so that they can perform optimally without being overstressed.

The sixth risk factor is vibration. Vibration from hand-held tools has been implicated in numerous hand and wrist disorders and many feel that it is a major contributor to cumulative trauma disorders.^{9,10} Better design of powered equipment or improved mounting of such equipment may reduce vibration.

While much has been learned about the risk factors which con-

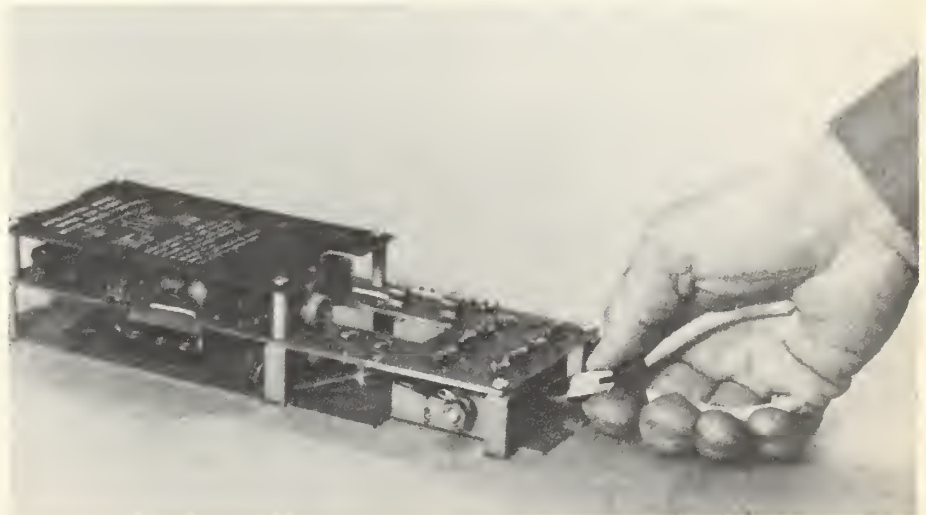


Figure 4. Poorly designed wire clipper. Note that when force is applied, it is transmitted to the base of the thumb.

I foresee the medical community and the engineering community working more closely together and establishing better lines of communication to provide effective interventions for the workplace.

tribute to the cumulative trauma disorders of the upper extremities, the condition nevertheless persists and is a major problem for industry. How then can we have some impact on the scope of the problem? As an ergonomics specialists in the field of occupational safety and health, I foresee the medical community and the engineering community working more closely together and establishing better lines of communication to provide effective interventions for the workplace. This process may be facilitated through techniques of job analysis whereby trained teams including physicians, safety and health professionals, manufacturing engineers, supervisors and workers jointly observe job tasks and apply appropriate ergonomic principles to improve job design. Video taping a job will assist in the observation and analysis and can provide a good means for review by an inter-disciplinary review team. As demands for quality of work life improve, application of ergonomic principles to the workplace will become more important, not only for control of cumulative trauma type injuries, but also to improve other conditions.

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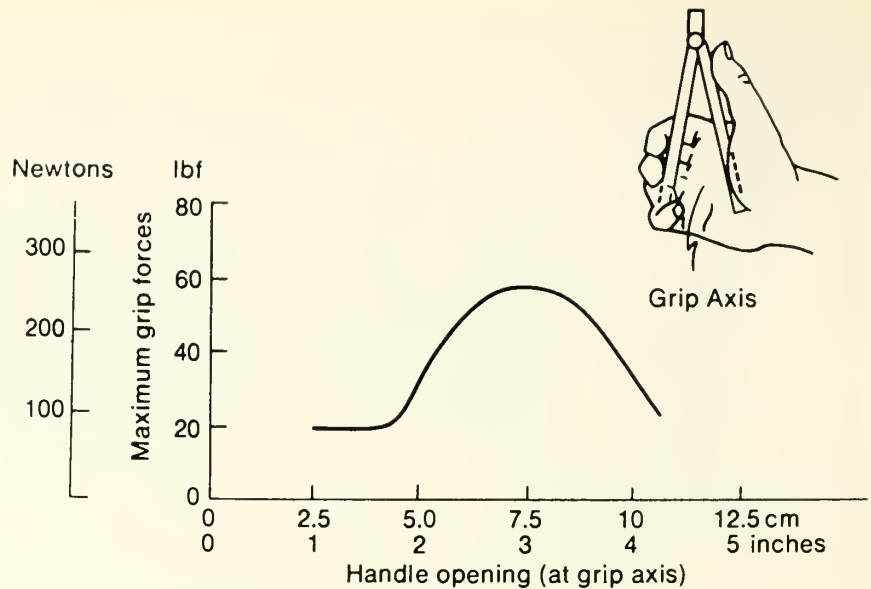


Figure 5. The graphic relationship between the handle opening at the grip axis of the tool and the average maximal grip force (for women).

References

- Armstrong TJ: An Ergonomic Guide to Carpal Tunnel Syndrome, American Industrial Hygiene Association, 1984, Akron, Ohio.
- Cannon LJ, Bernacki EJ, & Walter SD: Personal and Occupational Factors Associated with Carpal Tunnel Syndrome, Journal of Occupational Medicine, April 1981.
- Hadler NM, & Bunn WB: Work-related Disorders of the Upper Extremity Part 1: Cumulative Trauma Disorders — A Critical Review, Occupational Problems in Medical Practice, Volume 4, Issue 2, 1989, Medical Publication Inc., Wilmington, DE.
- McCormick EJ, & Sanders MS: Human Factors in Engineering and Design, page 307, McGraw-Hill Book Company, 1987.
- Armstrong TJ, Lifshitz Y: Evaluation and Design of Jobs for Control of Cumulative Trauma Disorders, Ch. 6. Ergonomic Interventions to Prevent Musculoskeletal Injuries in Industry, Lewis Publications, Chelsea Michigan, 1987.
- Cannon LJ, Bernacki EJ, & Walter SD: Personal and Occupational Factors Associated with Carpal Tunnel Syndrome, Journal of Occupational Medicine, April 1981.
- Wallersteiner UC: An Ergonomic Analysis of Upper Limb Cumulative Trauma Disorders, Canadian Occupational Safety, May-June 1985.
- McCracken W: Carpal Tunnel Syndrome: Ergonomics Takes the Upper Hand, OH&S Canada, Nov-Dec 1986.
- Wasserman D, Taylor W, Behrens V, Samueloff S, & Reynolds D: Vibration White Finger Disease in U.S. Workers Using Pneumatic Chipping and Grinding Hand Tools, I: Epidemiology (DHHS-NIOSH Publ. 82-118), Cincinnati: NIOSH.
- McCormick EJ, & Sanders MS: Human Factors in Engineering and Design, page 307, McGraw-Hill Book Company, 1987.

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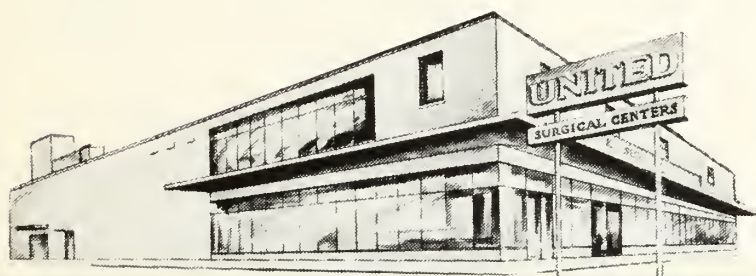
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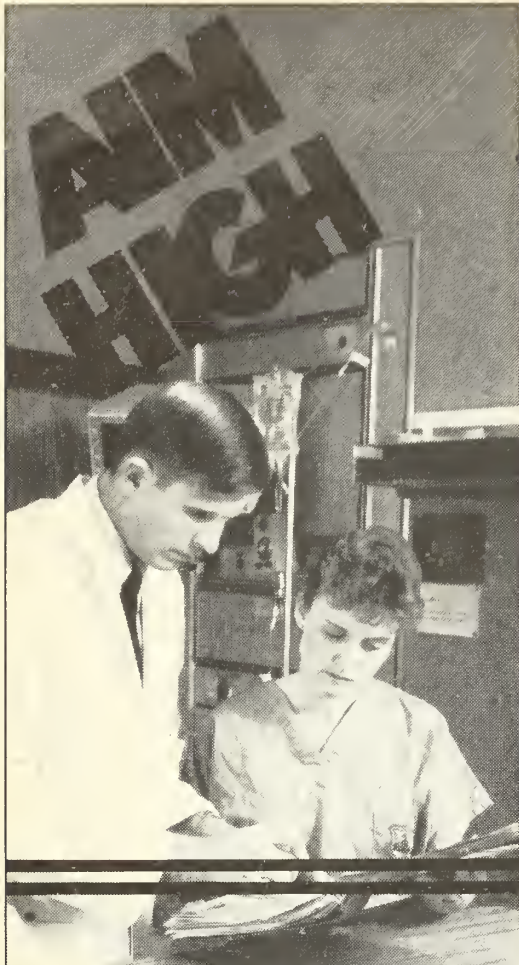
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Interdisciplinary Perspectives on Mechanisms and Management of Low Back Pain

David K. Ahern, PhD, *Moderator*

Duane Bishop, MD

Michael J. Follick, PhD

Melvyn Gelch, MD

Phillip Lucas, MD

John Parziale, MD

William Marras, PhD

Dianne L. Wilkin, PhD

Steven Wolf, PT, PhD

Chronic low back pain (CLBP) is one of the most pervasive and costly problems facing medicine today. In addition to personal suffering, CLBP accounts for a greatly disproportionate amount of consumer health care over-utilization, employee absenteeism, lowered work productivity, disability and compensation payments. Recent research in the area has called attention to the complex nature of the problem and the need for an interdisciplinary approach to identification and management. Toward this end, a panel of health care professionals with skill in the assessment and treatment of chronic pain was convened on November 17, 1988. Sponsored by the Institute for Behavioral Medicine in Providence and with funding from the National Institute for Neurological Disorders and Stroke, Stroke and Trauma Program, the purpose of the panel discussion was to bring together clinicians and researchers from distinctly different specialties but who all work with CLBP patients. Topics of discussion included etiology, current status of medical diagnostics and treatments for chronic pain, conceptual and systems issues, and directions for future research.

Moderator: What do you believe to be the critical signs or symptoms in a medical examination which would suggest the presence of disc or nerve root involvement?

Lucas: The presence of herniated disc or nerve root irritation is probably the easiest of all diagnoses to make for the physician treating individuals with lower back pain. One can often spot the individual with such a symptom complex as he/she walks into the examining room, and very often the history gives the diagnosis. The major complaint is that of leg pain, weakness or numbness. Any or all of these symptoms can be

present with nerve root compression.

There are two groups of patients that we see with nerve root involvement: A younger group, aged 20 to 40, that present with leg pain secondary to a herniated disc, and an older group, aged 50 and beyond, who present with leg pain secondary to spinal stenosis. Their complaints are different. The younger group complains of leg pain, and may also complain of numbness and weakness. Pain is exacerbated by standing or sitting. Relief can often be found in a reclined position. Symptoms begin acutely, often preceded by back pain, but

very often when the leg pain begins the back pain disappears. The older group with spinal stenosis generally complains of an achiness or weakness in the legs which is present with standing and walking and is relieved by sit-

ABBREVIATIONS USED:

CLBP: Chronic low back pain
CME: Continued medical education

CT: Computerized tomography

EMG: Electromyography

MRI: Magnetic resonance imaging

TNS: Transcutaneous nerve stimulation

ting down, much the opposite of the patient with an acute disc herniation. The leg symptoms are differentiated from those of vascular claudication in that the patient with spinal stenosis needs to sit down to get relief. He or she cannot stop walking or stand still.

On physical examination, the younger patient generally will report excruciating pain and show marked restriction in spinal mobility. He or she more often will show neurological deficit on examination of the extremities, with decrease in sensation, weakness, and reflex changes, and radiating pain with straight leg raise. The patient with spinal stenosis may show some spinal restriction, but generally this is in extension rather than flexion of the spine and the physical exam is remarkable only in the paucity of findings. Generally there is no evidence of neurological deficit. In a classic picture of nerve root involvement either due to stenosis or disc herniation, diagnostic studies such as a CT scan, MRI or myelogram should only confirm the diagnosis arrived at on the basis of the history and examination. It is very rare to have a false negative diagnostic test in a patient with nerve root involvement. On the other hand, patients with minimal clinical findings may have notable abnormalities on their CT scan, myelogram or MRI which may not be clinically significant. One must always keep in mind, especially in the surgical treatment of back pain and nerve root involvement, to treat the pa-

tient based on presentation of symptom rather than solely on the basis of diagnostic tests.

Moderator: What are the indications for surgical intervention in chronic low back pain?

Gelch: First, there is a major problem with the phrase "low back pain." I don't treat "low back pain" per se. I am a surgeon and operate for radiculopathy, that is, pain that radiates down the back and side of the leg along the distribution of the sciatic nerve. Low back pain can occur because of surgically-correctable conditions such as slippage of bones, spondylosis or spondylolisthesis. Radiculopathy can arise from tuberculosis or a metastatic process. Finally, low back pain can be secondary to instability of the spine because of some injury. If the spine were all vertebrae, that is, all bone, an individual wouldn't be able to bend at all. The spinal column is a flexible rod that permits bending and twisting. But where there's movement, particularly flexion, there is a significant amount of force or pressure applied to the spinal column. For example, if an individual bends over to lift an object, there is a tremendous acute pressure placed on the discs and the ligaments around them. And so when an individual tears a ligament somehow, the disc displaces. When a disc becomes displaced it pinches the nerve, transmitting pain down through the buttocks, legs, and occasion-

ally the groin. By examining the pattern of pain distribution, the clinician can identify the level of the involved disc.

In my practice I treat patients who have leg pain secondary to nerve compression. Those who have low back pain symptoms only are more appropriately treated conservatively. In those cases of low back pain secondary to spinal instability, an orthopedic surgeon such as Dr Lucas, who understands the mechanics of the back, would be the most appropriate treating physician. On the other hand, if the low back pain is derived from trigger points or lumbosacral or sacroiliac joints, a physiatrist such as Dr Parziale would be the most appropriate.

Low back pain is really only a description and not a diagnosis. A patient either has low back pain secondary to a specific working diagnosis or sciatica. If a patient has sciatica, he/she may require neurosurgical evaluation to rule out multiple sclerosis, herpes zoster, or diabetes affecting the nerve, and neurosurgical intervention may be required.

Moderator: Dr Gelch has raised some interesting points. The definition of terms is important to discuss. Dr Follick, would you differentiate acute and chronic pain conditions, and what the implications are for treatment of these two types of pain problems?

Follick: A clear distinction must be made between acute and

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chronic pain. In the context of an acute pain problem, the pain per se is considered as a symptom. Acute low back pain is the phrase used to describe pain that is less than three months in duration and typically is related to some injury. When considering chronic pain, the situation is quite different. Pain is not necessarily viewed as a symptom but rather often times is the primary problem. Chronic pain, in contrast to acute pain, is a complex phenomenon comprised of sensory, affective and evaluative components. Chronic pain is usually experienced daily and is pain that has persisted for an inordinately long period of time, usually six months or more, despite repeated medical interventions.

The mechanisms involved in the maintenance of chronic pain are hypothesized to be different than those for acute pain. In the case of chronic pain, psychosocial and/or environmental factors are considered to have a major influence on the clinical picture. Hence, treatment of chronic pain needs to be different than the treatment employed for an acute pain.

Moderator: Returning to the question of diagnosis, recently the field of medicine has witnessed major advances in technology. Diagnostic techniques have improved considerably with magnetic resonance imaging (MRI) perhaps as the best example. Dr Parziale, what additional information does MRI provide beyond Computerized Tomography (CT)? Also, would you comment on other techniques that are now

available for the diagnosis of low back disorders?

Parziale: Magnetic resonance imaging (MRI) allows excellent visualization of anatomy. It has certain specific advantages over CT, especially when evaluating soft tissues. With MRI the clinician can examine the sagittal plane quite clearly, something that is often difficult to do with CT. Additionally, the hydration status of a disc can be evaluated by MRI more readily than with CT. This aspect of MRI is important because in some disc syndromes, a dehydrated disc can in itself be a source of pain where a well-hydrated disc is less likely a source of discomfort. MRI can help in differentiating between fibrosis, hematoma, recurrent disc, and the patient who has a failed back surgery syndrome. A neurosurgeon would be less likely to operate upon a person who previously had back surgery if they were operating upon scar tissue only, since pain will most likely recur. If pain is related to a recurrent disc, that surgeon might be more likely to reoperate. MRI allows good visualization of the spinal cord and the spinal nerve root without intrathecal contrast. The sensitivity of the examination can be enhanced by weighing it differentially using T1 and T2 weights. That along with paramagnetic agents such as TV gadolinium can dramatically improve the contrast between the various soft tissue structures. Another advantage of MRI over CT is that MRI does not result in any radiation exposure. CT still has

an important place in evaluation of the patient with low back pain. In particular, CT is very good at examining bony structures. For fracture, displacement, or arthritis, CT is the preferable technique.

Is there still a place for myelography? Clearly, there is, but the role of myelography will be changing as we become more familiar with MRI techniques. Yet MRI is not without drawbacks. The MRI gantry is a narrow tunnel, and some patients become claustrophobic during testing. Also, MRI has certain contraindications such as its use with patients who have pacemakers or metallic implants.

Plain film X-rays have been used for many years and continue to be valuable as part of a baseline evaluation for low back pain. Thermography has been advocated by some although the reproducibility of the thermograph remains in question; thermography is not considered a particularly reliable diagnostic test at the present time. Electro-diagnostic studies such as EMG and nerve conduction studies can give excellent information about the integrity of the nervous system. Finally, somatosensory evoked potentials reveal the function of the spinal cord. To summarize, a variety of diagnostic techniques and studies as well as local injections and bone scans are available to help the clinician diagnose the causes of acute and chronic low back pain.

Moderator: There is some excit-

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ing work being done now in the area of the biomechanics of the lumbar spine. I would like to pose this question to Dr Marras first and then ask Dr Wolf to comment as well. Dr Marras, in your opinion, what are the critical biomechanical factors in low back pain?

Marras: Before I describe the biomechanical factors involved in low back pain, first let me give you a brief overview of the way I perceive the world. I like to divide the world up into both internal and external forces. External forces are those forces against which gravity works. In other words, if I'm going to lift a box, the force of gravity opposes the lift. Internal forces, on the other hand, are the muscular reactions to external forces and these can often become quite strong, as Dr Gelch had mentioned. It is important to look at the muscular involvement and that is often reflected by the motion of the back. I would like to come back to this point.

Wolf: It's remarkable that most of the low back pain patients we see don't have clear discogenic problems, nor is there clear evidence of radiculopathy. Thus, we have learned to ask a patient the critical question, "What activities exacerbate your pain and then show us those activities?" This question begins to address the biomechanical aspects of low back pain. We thought several years ago that one gained insight toward understanding the aberrations in movements in low back pain patients by evaluating bilateral paraspinal electromyographic activity to see how these

mirror-imaged muscles move relative to one another. While this approach has provided some insight into abnormal movements when compared to normal patterns, and also provided the basis for certain training and treatment strategies, it has not been the revelation that some clinicians would have liked. This is not surprising when we consider the complexity of the anatomy of the lower back. Presumably, most low back pain problems will govern the L4-L5 or L5-S1 vertebrae interspaces, and if we consider each as the minimum of four joints, and each moved by seven pairs of muscles on each side of the back, then any mechanical factors that produce an aberration in alignment can cause a change in the relative activity or tension in those muscles. As a result, there will be unequal pull upon the various bones. In turn, this excessive muscle tension can serve to reinforce the misalignment, thus leading to further pain.

A more exciting and promising approach to examining the importance of biomechanical factors is still in its infancy, and although we have touched upon this approach in recent years I think we are going to hear a lot more about it. This approach de-emphasizes electromyographic analysis and rather concentrates on kinematics; that is, the individual's ability to move through three planes during dynamic activities. There is accumulating evidence that kinematics may be a far more sensitive indicator of aberrations of movement in terms of pain than electromyography.

Marras: I agree totally with Dr

Wolf. Given my perspective as a biomechanicist, I want to determine what the low back muscles are doing to produce that force outside the body during dynamic movements. I think of this process in terms of a transfer function. What I mean by that is input versus output. In other words, I want to know what those muscles have to do to supply that counter force so as to maintain spinal equilibrium. As Dr Gelch mentioned, a particular lift may result in 2000 lbs of force exerted on the lumbar spine. From a biomechanical viewpoint, if an individual is holding 100 lbs some distance from the body, say a foot or two away, then a moment around the spine has been created which will be equivalent to the force times the distance. That moment must be counteracted by another moment, which is supplied by the muscle position relative to the spine. However, that muscle is only an inch or two away from the spine, so the forces have to be very, very great which is why there can be 2000 lbs of pressure on the spine. As Dr Wolf mentioned, there are several ways to evaluate the forces on the lumbar spine. One method involves electromyography to determine the amount of activity required to produce the necessary counterforce to the forces outside the body. Another method involves determining the net sum of that muscle activity, which is often reflected in motion patterns around the spine. In our laboratory, we have done studies that have demonstrated that there are dramatic differences in the motion patterns of individuals who are suffering

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from chronic low back disorders as compared to controls. I think that motion patterns are our "window to the world." This biomechanical approach determines exactly how all these muscles operate. However, there needs to be a word of caution. Presently, there are a number of back testing machines available on the market that measure these types of biomechanical parameters. It is very important to determine the net sum of the muscle activity during dynamic movement. Several machines claim they measure velocity parameters and motion components yet these machines may alter the motion so much that the clinician is no longer evaluating what the person has naturally developed over a lifetime of programmed learning of recruitment of those muscles. Several machines control the velocity of movement, which may be desirable when examining electromyography.

If the clinician is interested in examining the net sum of motion then the types of machines described above are not necessarily appropriate. There are other machines that let you use motion parameters as a dependent measure. The person is placed in a chair and then moved around in different planes. The motion patterns or the motion components are observed and analyzed for those with and without back problems. However, this type of machine also has limitations because the mechanics of the device may alter the motion of the back significantly. Usually the upper harness of these types of devices may weigh anywhere from 30 to 50 lbs which create huge moments of inertia. Thus, when an individual pushes against the device, the mass begins to move and will continue to move by itself even when the individual stops pushing against it. Clearly,

the clinician should carefully consider the advantages and disadvantages of the various types of machines, and the purpose for which it is intended, prior to making a purchase.

Moderator: Dr Follick alluded to the role of psychosocial factors in pain syndromes, especially as the transition occurs from acute to subacute, and ultimately chronic pain. First, Dr Bishop, what is the role of testing for organic signs when evaluating low back pain? And second, to what extent should the presence of significant emotional and psychosocial difficulties alter the medical approach to both assessment and treatment?

Bishop: Clearly clinicians need to conduct a careful assessment of the psychosocial components. There is compelling evidence that psychosocial factors are extremely important in the development of persistent pain conditions. George Engel and a number of other researchers promulgated the concept of the pain-prone individual. This research has suggested that a number of factors, in particular, individuals with a background of inordinate feelings of guilt, with a marginal adjustment to life and a high degree of problems, strong aggressive drives and those who experience loss or even the threat of loss are prone to developing persistent pain problems.

Other researchers have documented physical and sexual abuse in the backgrounds of individuals with chronic pain. They claim that these individuals have led miserable lives and are depressed. However, the research evidence suggests that most often depression associated with chronic pain is qualitatively different than major affective illness. Thus, we cannot claim that pain is simply a

symptom of an underlying major depression.

From a clinical perspective, the psychosocial examination will help the clinician make judgments about the course of treatment, which is a clinically important issue. It is also generally acknowledged that a central psychosocial component of chronic pain is depression. It is, therefore, important to determine the extent of depressive symptoms. For example, does the individual present with a history of chronic depressive symptoms or a depressive personality? Perceive the glass as being half empty rather than half full? Is the depression reflective of a psychiatric disorder? The presence of a chronic medical condition does not preclude the presence of a concomitant psychiatric disorder. Does it represent an adjustment to some chronic marital or family dysfunction, with an exacerbation of personality features as a result? And last, but not least, is the pain a result of depression secondary to the medication syndrome these patients often develop, the "junk syndrome" of multiple medications? The clinician must sort out these etiological factors, and remember that in a given patient several of them may be active.

Another approach is to consider different models, for example, a social learning theory point of view. Do operant or reinforcement factors account for pain complaints and behavior? Classical conditioning is also an important paradigm to consider. Patients frequently come to hospitals or treatment centers and have negative experiences because of unpleasant procedures, such as myelograms, and they may develop a conditioned fear as a result. These fears may persist and lead to full-blown phobias. Many of these patients have more phobias than we realize.

Also, modeling is an important process by which patients learn to respond to pain and illness. It is, therefore, important to determine whether these individuals have been exposed to family members or other individuals who suffered from pain or other disabling conditions and how they handled it. Hence, if we examine the patient from a social learning point of view, and find positive evidence, then this information will help to determine the kind of treatment to be provided.

The second model is adaptation. As clinicians we often overlook the individual's preferred coping strategy. Some people read books when they get upset, some people go out and chop wood. If you're a wood chopper, and you develop a chronic back condition, you not only have the back problem, but you have lost your coping strategy, whereas the person who reads the books may actually be able to make use of that activity to overcome or modulate the pain problem. The other aspect to consider within the adaptation model is the presence of maladaptively used defense mechanisms. For example, is the individual someone who tends to somaticize, ie, express distress in physical symptoms, overly focus on bodily functions or displace conflicts onto their body?

To summarize, there are many psychosocial contributions to chronic pain and several models we can use to assess them. We need to evaluate carefully in order to choose the most appropriate treatment.

Moderator: The assessment of low back pain is compounded further by the fact that there are significant socioeconomic implications when an assessment is conducted of a chronic pain patient. The terms that describe limitations are not understood clearly

and, consequently, often confused. Dr Parziale, would you comment on and distinguish among the terms impairment, disability and handicap?

Parziale: The terminology is often misused in clinical practice. The World Health Organization has developed standard definitions for impairment, disability and handicap. Impairment is an abnormality of psychological, anatomical or physiological function.

Disability is a loss of functional capacity at an individual level. Handicap is the resultant disadvantage of the disability which can take various forms. It can assume socioeconomic, vocational, or cultural forms. Let me give you an example of how these terms may be distinguished. A young man presents with spondylosis or spondylolisthesis in his lumbar spine found on routine X-rays. That individual may be symptomatic or asymptomatic. If he's asymptomatic, he has an impairment; there is a structural abnormality, but there is no resultant disability. If this man is symptomatic, he may have very little disability if he is employed in a fairly sedentary type of job and has the types of coping strategies that Dr Bishop spoke about for his pain problem. On the other hand, if this individual is a professional football player who has significant pain from this impairment of his lumbar spine, he may have significant disability which will then give rise to a resultant handicap. He may not be able to pursue his vocation, which would then lead to a cultural and socioeconomic hardship.

Moderator: I'd like to shift our focus now to treatment questions and ask Dr Gelch, what are the criteria for surgical interventions following an initial laminectomy?

Gelch: As a neurosurgeon, I'd like to comment first about the evaluation of psychological/psychiatric problems in this population. There is no question that chronic pain is very commonly associated with depression. Many of the medications used for pain such as Percodan may mask an underlying depression. But my experience as a neurosurgeon for many years has made me aware of the potential for a neurophysiologic basis for depression in these patients. For many years, I had performed a lumbar laminectomy for a pinched nerve which relieved leg pain but the patient would be discharged with depressive symptoms. For the past 4-5 years, I've been prescribing high doses of steroids post-operatively to address these symptoms, with favorable results. In many cases, the depression resolves within 24 hours. In these cases, the depression is not solely functional but rather the fact that the chronic pain produces adrenal insufficiency. Often times now when we conduct a workup for depression in the hospital, we determine ACTH levels and perform other hormonal tests to determine if there is any underlying physical cause. It is my opinion that many of these people with chronic pain, because of the stressful nature of the condition, develop adrenal insufficiency. These patients become depressed and slow down in their activities. In turn, they become so concentrated on their back pain and problems because they are afraid of more pain that they develop a chronic pain syndrome which then becomes very complicated. So it is important to rule out any physiologic basis for the depression that might be correctable.

As I mentioned earlier, surgery is indicated only if there is evidence of radiculopathy. There are

only two types of disc that are operative. One of the two types of disc is called the ruptured disc, that is, a disc that literally breaks into pieces, like a "volcano erupting." It's not a herniated disc, it's not a slipped disc, it's not a bulging disc. In a published study in the *Journal of Spinal Disorders*, researchers at the University of Pennsylvania and Pennsylvania Hospital conducted a retrospective study on their patients who were carefully selected for and underwent surgery.¹ They claimed that 95 per cent of these patients experienced good to excellent results from lumbar disc surgery. Clearly, careful screening and selection is crucial to achieve this high a success rate. The second type of disc is one that becomes displaced beneath what is called a posterior longitudinal ligament. These are ligaments that keep this soft, spongy material in place. If a tear occurs the disc can then come out through the ligament. Oftentimes a disc comes out beneath the ligament over the bone and cannot get back into place. It is likely that there are discs that "slip out and slip in" and this process is one of exacerbation and remission of pain. Indeed, most individuals with acute pain get better regardless of the treatment provided. But we do know that there are two types of disc, the ruptured disc that breaks into pieces and the incarcerated disc which is displaced and pinches a nerve to the extent that the body cannot accommodate. One can observe that the lumbar spine becomes flatter, with a disappearance of lumbar lordosis in these patients. That is nature's way of moving the disc away from the nerve. It causes a flattening of the back. But there is a limit to what the body can do to accommodate to a disc that is displaced and compressing a nerve. So we do operate only for those two types

of discs. Ordinarily, further exploration is not appropriate. The diagnostic techniques that are available, as Dr Parziale noted, are quite good. With the combination of CT, MRI, and myelography, one you can obtain as high as 97-98 per cent diagnostic accuracy. However, these tests can be costly. Most importantly, the physical examination is essential in determining whether or not a patient is likely to be a candidate for surgery. The techniques noted above are then used to confirm the diagnosis and help pinpoint the exact location of the defect. With regard to repeat surgery, an operation should not be performed solely to remove scar tissue because it simply will recur. When you cut scar tissue, what do you leave behind? You leave blood. What does blood form? Blood forms scars. Basically you would never operate just for scar tissue. However, there are cases where a bone compresses the nerve root. In these cases, a second and even third operation may be necessary. Some patients do improve with a second operation, between five and ten per cent, but as is the case for initial surgery, one has to be very careful that there is a clear disc problem and not simply scar tissue. Unfortunately, if a nerve has been compressed for some time, alterations in the nerve can occur that may never be correctable, even with decompression.

Moderator: As an alternative to surgery, a number of treatments have been developed. Dr Parziale, would you comment on the different non-invasive treatments available for chronic low back pain?

Parziale: Actually, there are many treatments that should be considered for low back syndromes prior to performing surgery. Generally,

it is acknowledged and, I believe most surgeons would agree, that there are relatively few and fairly discreet indications for low back surgery. Surgical intervention is often restricted to problems such as changes in bladder function, acute pain that has been caused by severe tissue compression and progressive neurologic deficit. Typically, the CLBP patient that we would see in our Rehabilitation Medicine Practice is one who does not have these specific clinical signs. Treatment may begin with an education program, usually coupled with a low back exercise program. If radiculopathic changes have led to weakness in the lower extremity, then usually lower extremity exercises are provided as well. The type of low back exercise that is recommended may vary from institution to institution and therapist to therapist. There is good evidence though that for many individuals who present with acute or subacute low back pain, extension exercises, such as the McKenzie techniques, can be very effective in reducing discomfort. Williams flexion exercises have been prescribed routinely for low back pain and are appropriate for many patients. Traction is often applied to theoretically reduce the tension upon the disc to the point where actual distraction of the two bodies is achieved. Substantial force needs to be applied to accomplish this objective, in the range of 50 per cent of body weight, and the force has to be applied to the pelvis keeping the upper torso fairly stable. Consequently, traction is difficult to apply consistently well and may produce additional pain. Ultrasound has been used to heat soft tissues, but may be ineffective in many conditions. In cases of small tumor or prior laminectomy ultrasound is actually contraindicated because of the potential

for additional damage. Superficial heat can be effective at reducing paraspinal muscle spasms. Ice treatments may be used for the same reason. The other treatments that are applied in addition to exercise, traction and heat or ice modalities include electrical stimulation to reduce paraspinal spasm. Electrical stimulation can fatigue a muscle that is in severe spasm and consequently can produce relaxation of that muscle which can lead to a reduction in pain. Transcutaneous nerve stimulation (TNS) units can be used to relieve pain as well. The use of lumbar or lumbosacral corsets can increase intra-abdominal pressure and thus relieve intradiscal pressure.

Perhaps the most promising concept developed in treating pain syndromes on a long-term basis has been the idea of the "neutral" spine,² promulgated by Dr Jeffrey Saal. The objective is to move a patient through various ranges of motion and define the position of the spine that is most comfortable, which is not always what is the normal lumbar lordosis. The patient is taught to maintain that neutral position of the spine whenever they change from a standing to sitting position, sitting to standing, supine to sitting and/or lifting objects. Hence, when a transition is made, most of the force is applied to the legs rather than to the low back region. This approach represents an important theory in the rehabilitation of low back pain patients.

Moderator: Dr Wolf, do you want to make any additional comments on treatment alternatives?

Wolf: Well, I agree with Dr Parziale that there has been an attempt to develop treatment meth-

ods based upon normalization of the spinal alignment. Considerable research has been conducted utilizing paraspinal EMGs during static postures and dynamic movements with the goal of understanding the forces on the lumbar spine during these activities. I have concern with most thermal modalities. Under the appropriate conditions, either heat or ice can reduce muscle spasm; but the undeniable fact is that the cause of the spasm is often indeterminate and those spasms will persist and represent themselves as long as that imbalance in muscles remains. Unfortunately some proponents of mobilization techniques, including manipulation of the spine and gentle mobilization based upon palpation and reorganization of misaligned spinal segments, have not adequately documented the scientific validity of these approaches. In my experience, and perhaps for some of you in this room, very favorable results have been obtained with mobilization techniques. However, it is very difficult to document the validity and efficacy of this approach. With regard to electrical stimulation, particularly TNS, we have had some experience at my institution regarding its utility as a treatment technique. In most cases, patients do very well while they are under the TNS treatments along with other interventions, but as soon as the applications are relegated to the patient, out of the context of the clinical setting and when these patients are subjected to a variety of other factors over which we have no control, the benefits of this form of stimulation decrease considerably. Thus, I would say that electrical stimulation to block pain has a limited role in the total comprehensive care of back pain patients.

Moderator: A number of our panelists today have commented on the association between chronic pain and depression. Dr Bishop, would you comment on the role of antidepressants in the treatment of chronic pain.

Bishop: I think the term antidepressant is somewhat of a misnomer. These drugs affect neuronal transmission and vary in their actions and side effects depending on which enzyme systems they affect. Some of the earlier generations of these drugs affected many receptor systems. Presently, there are antidepressants available that affect only specific receptors.

Antidepressants have other effects. For example, some are very potent analgesics and can be used in conjunction with other analgesics to maximize the desired analgesic effect. Amitriptyline would be an example. Imipramine is a very effective, fast-acting antispasmodic (within 24-48 hours), quite different than the time-line for its antidepressant effect, which typically is about two weeks. The antidepressants are also potent in reducing anxiety. Clearly, they are effective in the treatment of the neuro-vegetative symptoms of depression such as sleep and appetite disturbance as well as other symptomatology such as negative attributions and the negative/pessimistic view of the world that I mentioned earlier. The antidepressants are also useful with patients who suffer from obsessive-compulsive disorders. Many chronic pain patients present with very fixed and rigid pain complaints, some of which take on a very strong, obsessive quality. In summary, antidepressants have an important role to play in the treatment of pain syndromes and the choice is determined by the symptom pattern to some extent. As I men-

tioned earlier, the promise for the future is further specificity of action and this in turn will increase our knowledge of the psychophysiological correlates of complex pain problems.

Moderator: Clearly, CLBP is a major health care problem that has stymied attempts at diagnosis and treatment. Because of its complexity and recalcitrance, CLBP has an enormous socioeconomic impact. Dr Follick, would you comment on CLBP and the Worker's Compensation System.

Follick: In the past few years, problems with the Workers' Compensation System have received a great deal of attention, oftentimes with a lot of finger pointing. Since CLBP is one of the most frequent and costly work-related injuries, it is an issue of great concern. Physicians, attorneys and employers at various times have been accused of contributing to the failure of the compensation system which was to meet the needs of patients and society at large. It is my opinion that there are a multitude of factors involved, each contributing to the problem. As a society, we have to consider the total system. There is little or no benefit gained from finger pointing; rather it serves to obscure the complex nature of the problem and movement toward some resolution. Another element that is often not addressed or recognized but which is part of the system, particularly in Rhode Island, is the presence of an "entitlement syndrome" among workers. According to this philosophy, once an individual is injured, he or she is *entitled* to receive benefits until death or unless a cure is obtained. This mind set contributes to the magnitude of the compensation problem.

With regard to the economic

costs of work-related injuries, approximately 75 per cent of the costs are the result of indemnity payments, with the remaining 25 per cent attributable to medical costs. Hence, the longer patients remain out of work, the greater the cost. In a ten year period between 1976 and 1986, Workers' Compensation costs rose 355 per cent. In this same time period, the average weekly pay rose 96 per cent. So you are looking at a 16.5 per cent increment in the cost of Workers' Compensation compared to a 7 per cent annual increment in the weekly wage. These statistics tell the story of a system that has spiralled out of control. Unfortunately, many patients become caught in the system because of inefficiency. In many cases there is no definitive treatment plan, or endpoint. Although I don't want to single out any one profession, those health care providers that carry on treatment indefinitely without objective evidence of improvement perpetuate the problem. It is my opinion that the time has come where people who are paying the freight for the health care system, ie, corporate America, are not going to ask anymore for changes in the system. Rather, they are going to demand a change because of limited financial resources. Thus, the system is sorely in need of overhaul with the goal of providing quality care while at the same time reducing cost.

Moderator: At this point, I would like to pose one question to all of the panel members. What are the major etiologic factors in chronic low back pain?

Parziale: Actually, there are many factors involved in low back pain. Some have been examined more carefully than others but, in particular, the data collected in re-

lation to the occupational health situation are quite compelling. The research evidence indicates that for those individuals who have suffered an on-the-job injury, certain types of work activities and the association between physical status and work activity can place them at high risk for low back pain. Those individuals who perform heavy labor, especially repeated, heavy lifting, are at risk for low back pain. One study that compared heavy vs moderate vs light manual work with the incidence of low back injuries found that those persons who are in heavier work areas have about a 2/3 higher rate for low back injury than those persons who are in moderate or light types of work activities. The frequency of load handling is another factor which can increase the risk for low back pain. The match of an individual's strength with the physical demands of the task is also important. For example, a 170 lb man who lifts a 50 lb box several times a day is at more risk for experiencing an injury compared to a 200 lb man who also lifts several times a day because of the difference in weight and strength. Prolonged sitting or standing, assymetric lifting or twisting activities can also place individuals at higher risk for low back injuries. Many other factors that I'm sure the panel will comment on such as alcohol and tobacco use, various psychological disorders and satisfaction with the job, combine to increase an individual's risk for low back injury.

Gelch: I agree with Dr Parziale. Clearly, there is no one etiologic agent in low back pain.

Bishop: As I mentioned earlier, in the context of a low back injury, psychosocial factors con-

tribute to the transition from an acute phase into a chronic phase.

Lucas: This issue is very controversial. At the present time, we really don't know the cause. There are many etiologic theories that have been proposed and we must ascribe to some theory in order to guide the treatment we provide. One must remember that back pain is a symptom, not a disease, so it is important to try to determine an appropriate working diagnosis. One can hardly develop a treatment program if, in fact, there is no working diagnosis. As has been mentioned today, low back pain can originate from many sources including muscle strain, injury to the sacroiliac joint, herniated disc or facet joint derangement. It is very difficult, if not impossible at times, to pinpoint the precise causal factor. If we just limit ourselves to the spinal column for a moment, I will propose what I consider to be important etiologic factors. The theory I ascribe to was developed by Kirkaldy-Willis in Canada.³ According to this theory, lower back problems develop as a result of a natural degenerative process that begins at an early age, 18-20, when biochemical changes start to occur within the disc. These changes, in turn, lead to alterations of biomechanical processes in the way the disc responds to the various stresses of everyday life. As the disc undergoes degeneration, it becomes less able to protect the facet joint, which in turn, begins to set arthritic changes in motion. This theory is consistent with the clinical course where, as Dr Gelch mentioned, symptoms wax and wane. Initially, there's an injury, perhaps secondary to disc degeneration. In response to this injury, the body responds in a protective fashion which permits healing;

hence, initial symptoms resolve. This explains, I think, why most people with back problems get better. There is a natural healing process. It is only when an event occurs that the body cannot respond to that a chronic process begins to develop. This theory can also be useful to patients in terms of helping them understand the fluctuating course of the problem. There are additional factors that Dr Parziale and Dr Bishop alluded to that effect this natural history. Anything that effects the nutrition of the disc is going to accelerate the degenerative process so that if the blood supply to a disc is compromised in some way, there is likely to be a more rapid change in the degenerative process. It has been demonstrated in animal studies that exposure to cigarette smoke decreases diffusion of nutrients into the disc, and patients who smoke (compared with nonsmokers) have a higher incidence of back pain. Another relevant factor is the amount of motion or activity of the individual. Motion actually helps the disc by increasing the diffusion of nutrients and slowing the degenerative process. Finally, genetically determined body type and biomechanical characteristics are also contributing factors.

Marras: To expand on Dr Parziale's comments, there are data that support the contention that a third of the back injuries that occur in this country can be eliminated through preventive measures in the workplace. Cumulative trauma, a concept that has not been mentioned today, is in my opinion a major factor in the etiology of low back disorders. It is the repetitive wear-and-tear that is responsible for the biomechanical degenerations that are often found in these patients, as described by Dr Lucas. For exam-

ple, if I take a coat hanger and try to pull it apart with my bare hands, I would not be able to. It can't be broken apart. But if the same coat hanger is worn by bending and twisting it at the same point over and over, eventually it will break. With this process, the metal heats up, becoming more brittle. The weakened coat hanger provides a gross analogy to what happens in the body. It is that repetitive wear-and-tear and strain placed on a particular joint during the performance of work, coupled with natural degenerative changes, that, in my opinion as a biomechanicist, is responsible for many of the back injuries today. Prevention of these problems can be accomplished through the application of proper ergonomics. Ergonomics is the study of human factors and matching the workplace to an individual's capabilities. Dr Parziale mentioned the importance of matching workers with the physical demands of their jobs. I think we should go one step beyond and make sure we design the job so that anybody could do it, not just certain people. Then we do not have to worry about worker selection, and through proper engineering techniques and biomechanical analysis, this task can be accomplished today. Another point I would like to comment on is not just the risk associated with heavy lifting but the manner in which an individual conducts these lifts, especially acceleration of the back during a lift. Motion patterns play a very big role since force is equal to mass times acceleration. When either heavy or light loads are moved very rapidly, an impulse is generated on the spine. This impulse plus the co-contraction of the muscles cause impulse loadings on the spine that are substantial. Thus, it is not surprising that injuries occur particularly for those people with de-

generation and other contributing factors.

Follick: Clearly, there are multiple etiologic factors; organic, biomechanical, environmental and I want to comment on another important source, psychosocial. The psychosocial aspect of pain syndromes, as Dr Bishop stated, often times distinguishes acute from chronic and, therefore, the treatments for these conditions must be different. That is not to say that psychosocial factors are not related to acute injury. Indeed, they influence the acute injury rate. Not only are there the biomechanical factors that Dr Marras described but accident frequency can be influenced by an individual's state of mind, level of depression, behavior and job satisfaction. Another factor is malingering, although frank malingering is surprisingly low in prevalence. The last point I want to make is the impact that psychosocial factors have on the maintenance of disability. Unfortunately, it is not uncommon for a detectable organic defect, say nerve root entrapment, to be corrected at least from a strictly surgical perspective, and yet the disability persists. In this case, psychosocial and behavioral conditioning variables are likely to play a major role in determining the patient's functional disability status.

Wolf: I think the etiological factors of low back pain are as diversified as human behavior. What Dr Follick referred to as psychosocial factors, I consider more cultural factors. The manner in which we respond to back pain in our society, I believe, helps to explain why we have the problem of chronic pain behavior, compared to other cultures. With reference to other factors, certainly

there is the likelihood of a genetic predisposition to back injuries. Some individuals are going to have "bad backs" whether they want to or not; it is probably inevitable, given a genetic predisposition and the presence of precipitating factors, many of which have been mentioned today. Finally, with respect to biomechanical issues, I agree that many back injuries are related to the work place. Elements such as fatigue, lack of conditioning, and overexertion all contribute to the probability of an injury and, quite frankly, that blends into the notion of repetitive trauma. From this perspective, clearly, the better prepared, physically and emotionally, an individual is, the less likely the risk for low back injury. Pertinent to this point is the importance of preparation for work or what is referred to today as "work hardening." All too often we consider work hardening only after an injury has occurred. I would recommend the establishment of very specific conditioning programs geared at prevention rather than limited only to post-injury intervention.

Moderator: To summarize, although we are uncertain about the exact etiology of chronic low back pain syndromes, our panelists today have identified most of the likely factors. I would like to take an opportunity to thank our panelists at this time.

All recommendations or suggestions for use of drugs, devices or techniques contained in this panel discussion reflect the opinions of the discussion participants. No responsibility or liability in presenting this information is assumed by the editors, the publisher, or the accrediting institution.

References

- ¹ Garfin, S.R., Glover, M., Booth, R.E., Simone, F.A. and Rothman, R. (1988), Laminectomy: A review of the Pennsylvania Hospital experience. *Journal of Spinal Disorders*, 1(2):116-133.
- ² Saal, J. (1988), Diagnostic studies of industrial low back injuries. *Topics in Acute Care and Trauma Rehabilitation*, 2:31-49.
- ³ Willis-Kircaley, W.H. (1988), Managing low back pain, Churchill Livingstone, New York, 1988.

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The closed-book, multiple-choice examination that follows this panel discussion is designed to test your understanding of the content based on the educational objectives listed below.

EDUCATIONAL OBJECTIVES

1. Identify etiological factors in the development of chronic low back pain.
2. Identify factors involved in chronic low back pain from different professional disciplines.
3. Identify factors most appropriate for both surgical & non-invasive treatments for low back pain.

CME Questions

The proceeding was a panel discussion of experts in the area of low back pain representing several different disciplines. Please answer the following questions based on the information provided in the text above, but do not refer back to the text. Please note that there is only one correct answer to each question.

1. When pain is considered to be the primary presenting problem rather than a symptom, it is most likely
 - a) recurrent
 - b) acute
 - c) psychological
 - d) chronic
 - e) organic
2. Computerized tomography has advantages over magnetic resonance imaging when examining
 - a) the saggital plane
 - b) bony structures
 - c) dehydration of a disc
 - d) fibrosis
 - e) soft tissue
3. MRI might be the diagnostic tool of choice in all but which of the following instances, when a patient has
 - a) a hematoma
 - b) a pacemaker
 - c) an undiagnosed tumor
 - d) diabetes
 - e) a recurrent disc
4. At the present time, some of the most useful diagnostic measures for low back pain are all but the following
 - a) X-ray, CT scan, MRI, thermography
 - b) CT scan, MRI, X-ray, myelogram
 - c) bone scan, X-ray, CT scan, MRI
 - d) MRI, evoked somatosensory potentials, X-ray CT scan
 - e) local injections, x-ray, CT scan, MRI

5. According to some researchers in biomechanics, which of the following is a more sensitive indicator of aberrations of movement secondary to pain?

- a) electromyography
- b) kinematics
- c) bone scan
- d) evoked somatosensory potentials
- e) angular measurement

6. From a biomechanical perspective the most important factor in low back pain is (are)

- a) electric activity of the muscles
- b) biofeedback monitoring
- c) calculations of muscle mass
- d) force times distance
- e) motion patterns

7. Which of the following statements is false?

- a) Personality and coping patterns frequently determine whether an acute back injury will become chronic.
- b) The central psychosocial issue in pain is depression.
- c) Individuals from families with passive and dependent characteristics are more likely to be pain prone than those from aggressive, hostile backgrounds.
- d) Over-reliance on medication can produce depression.
- e) Research suggests that depression associated with chronic pain is qualitatively different from a major affective disorder.

8. A model which examines an individual's style of coping with life stress prior to the onset of a chronic illness condition is

- a) biobehavioral
- b) adaptation
- c) social learning
- d) psychological
- e) William's

9. According to the World Health Organization, abnormality of psychological, anatomical or physiological function is termed

- a) impairment
- b) chronic pain syndrome
- c) disability
- d) handicapped
- e) dysfunctional

10. According to the panel discussion, a patient who might be the least likely can-

didate for surgery for low back pain would be one who presents with

- a) injury to a nerve root
- b) spinal stenosis
- c) a ruptured disk
- d) a herniated disc
- e) an incarcerated disc

11. Physical therapists most frequently will observe the absence of a normal lumbar lordosis in cases involving

- a) sciatica
- b) ruptured disc
- c) spinal stenosis
- d) torn ligament
- e) pinched nerve

12. In cases involving a bony structure compressing a nerve root, what percent of second surgeries are likely to be successful?

- a) 5-10%
- b) 25-35%
- c) 50-60%
- d) 97-98%
- e) none of the above

13. In the majority of cases, which of the following would be the least preferential noninvasive treatment for pain following surgery?

- a) TNS
- b) heat
- c) physical therapy
- d) ultrasound
- e) medication

14. According to Dr Jeffrey Saal, the "neutral" spine refers to

- a) anatomically normal lumbar lordosis
- b) the position of the spine which is most comfortable
- c) one which has not had radical surgical intervention
- d) zero degrees forward flexion
- e) none of the above

15. Two of the major factors adversely affecting the Workers' Compensation system in the State of Rhode Island are

- a) inadequate funding by the State legislature
- b) the over-involvement of various medical disciplines
- c) the under-representation of injured workers by competent attorneys
- d) the lack of a definitive treatment plan or end point for most injured workers
- e) the presence of an "entitlement syndrome" among workers

- a) (1) and (4)
- b) (2) and (3)
- c) (3) and (4)
- d) (4) and (5)
- e) all of the above

16. With regard to economic costs, what are the relative percentages of indemnity payments to medical care costs?

- a) 20, 80
- b) 80, 20
- c) 50, 50
- d) 40, 60
- e) 60, 40

17. Which of the following have not been posited as etiological factors in the development of chronic low back pain?

- a) cigarette smoking
- b) motion increases the diffusion of nutrients to the disc but can speed up the degenerative process
- c) genetically determined body types can be a contributing factor
- d) psychosocial factors can assist in the progression of an acute into a chronic condition
- e) aging has been identified as a key factor in the development of back pain

18. It has been estimated that what percentage of injuries in the workplace could be eliminated through preventive measures?

- a) 10
- b) 30
- c) 50
- d) 60
- e) 70

19. The study of matching the workplace to an individual's capabilities is referred to as

- a) human dynamics
- b) human engineering
- c) work capacity
- d) ergonomics
- e) work hardening

20. Indicate which of the following are true:

- 1) Imipramine is an example of a fast acting anti-spasmodic which has a delayed effect upon an affective condition.
 - 2) Psychosocial factors can influence acute back injuries by being related to such things as types and frequency of accidents.
 - 3) Outright malingering is of surprisingly low prevalence in the incidence of low back pain.
 - 4) Psychosocial factors have perhaps their greatest influence upon the maintenance of disability.
- a) (2) and (4)
 - b) (3) and (4)
 - c) (2), (3), and (4)
 - d) (1), (2), and (4)
 - e) All of the above

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Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

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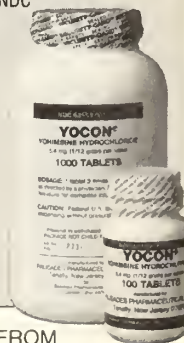
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

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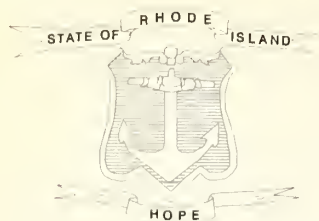
References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

The Rhode Island WIC Program

The Rhode Island WIC Program is a state-administered program funded under the federal Special Supplemental Food Program for Women, Infants, and Children. It provides nutrition counseling and nutritious foods to women who are pregnant, postpartum, or breastfeeding, to infants, and to children under the age of five. The purpose of WIC benefits is to supplement good health care in order to prevent nutrition-related health problems among low-income mothers and their children. WIC services are provided at 14 locations throughout Rhode Island, including hospitals and local health centers. Participants must be Rhode Island residents, have limited income, and be at some documented nutritional or medical risk.

The program's client population includes many of those at high risk of poor birth outcomes or growth deficiencies. Minority groups, who are over-represented among low-income residents, are served in larger proportions than they appear in the state's population, with Blacks, Hispanics, Asians, and American Indians comprising over 40 per cent of partici-

pants (Figure 1). Also, the program serves higher proportions of infants, who are more likely to be at nutritional risk, than of women or older children (Table 1).

From 1974 to 1983, WIC served an increasing number of clients, with essentially stable participation after 1983 (Figure 2). Most recently, funding levels have not kept up with inflation, but the program has been able to increase participation with funds received under a rebate agreement with Mead Johnson, makers of infant formula under the brand names *Enfamil* and *ProSobee*. Under the contract with Mead Johnson, WIC programs participants use these brands of formula unless otherwise indicated by allergy or medical intolerance. The WIC Program is given a discounted price for these brands, with the discount returned to the program as a rebate. In 1990, the rebate program will allow WIC to serve an additional 2,500 clients.

Rhode Island physicians play an important role in the provision of high-quality services to WIC clients. Physicians refer patients to the program and document nutritional and medical risks. For infants

who are allergic to or medically intolerant of the contract brands of formula, physicians may prescribe alternative brands. To date, physicians have kept exceptions to one per cent of the 4,000 infants on the program, allowing the rebate program to augment WIC participation by nearly the maximum possible number of additional recipients.

Reference: The National WIC Evaluation: Evaluation of the Special Supplemental Food Program for Women, Infants, and Children. *American Journal of Clinical Nutrition* 48(2):389-519 (Supplement, August 1988).

Table 1. WIC Program Enrollment and Per Cent Penetration by Eligibility Category, Rhode Island, November 1989.

Eligibility Category	Number Eligible	Number Served	Per Cent Penetration
Women	6,741	2,991	44.4
Infants	5,393	3,633	67.4
Children	19,520	9,130	46.8

Figure 1. Distribution of WIC Program Participants by Race/Ethnicity, Rhode Island, September 1989.

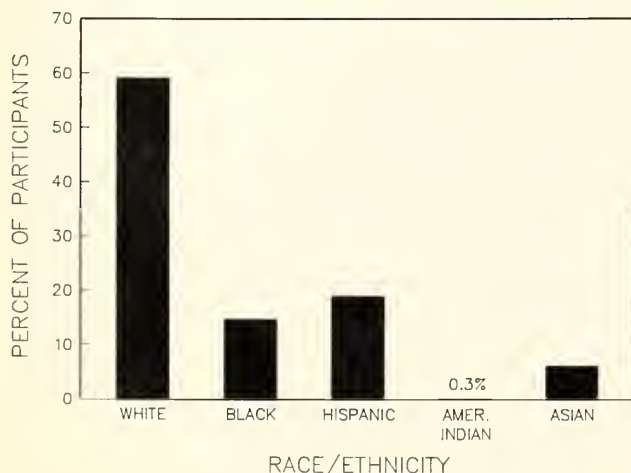
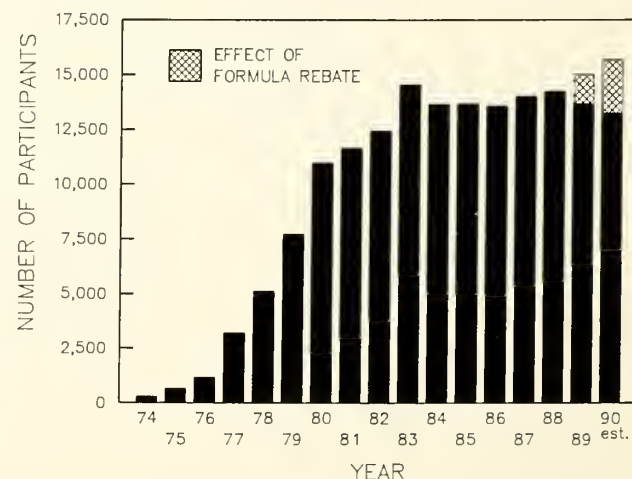


Figure 2. WIC Program Participation, Rhode Island, 1974-1990.



Submitted by the Office of Supplemental Nutrition (WIC), John L. Smith, MSW, Chief. Health by Numbers is edited by Jay S. Buechner, PhD, and William J. Waters, Jr, PhD.

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period September 1989	12 Months Ending with September 1989	
	Number	Number	Rates
Live Births	1,383	14,990	15.1*
Deaths	720	9,690	9.8*
Infant deaths	(13)	(146)	9.7†
Neonatal deaths	(11)	(113)	7.5†
Marriages	1,183	8,305	8.4*
Divorces	291	3,638	3.7*
Induced Terminations	644	7,840	523.0†
Spontaneous Fetal Deaths	135	1,153	76.9†
Under 20 weeks' gestation	(117)	(1,014)	67.6†
20+ weeks' gestation	(11)	(111)	7.4†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

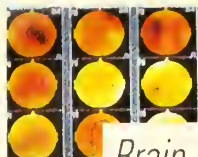
Underlying Cause of Death Category	Reporting Period June 1989	12 Months Ending with June 1989		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	248	3,477	350.2	4,582.5
Malignant Neoplasms	203	2,404	242.1	7,680.0
Cerebrovascular Diseases	47	596	60.0	1,120.0
Injuries (Accident, Suicide, Homicide)	30	422	42.5	9,982.5
COPD	24	311	31.3	451.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.



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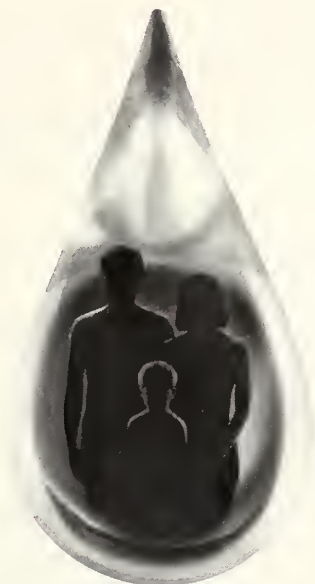
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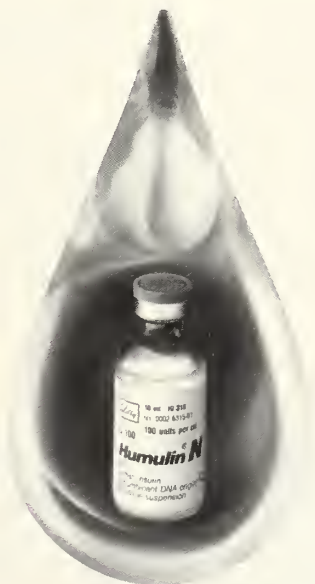
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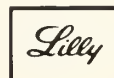


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THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME I
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (January, 1940)

The *Journal*, some 16 pages in length, is edited by Dr Albert H. Miller with Associate Editors, Drs Charles Bradley, William Buffum, Alex Burgess, Francis Chafee, John Ham, John Helfrich, Ernest Thompson and George Young.

The lead article is entitled "Anesthesia for the Benefit of the Patient" and represents a distillation of commentaries by Drs A. H. Miller, M. Saklad and J. A. Hayward in a symposium presented before the 128th Annual Meeting of the Rhode Island Medical Society held in June, 1939. The article begins with the observation that, "During the 87 years which have elapsed since the introduction of etherization, more than 500 agents for producing surgical anesthesia have been recommended and tried. While most of these agents have proved so inefficient or so dangerous that they have shortly been abandoned, more than 50 agents are in use at the present time and these agents are administered by no less than 25 different methods." The paper considers first premedication, then the anesthetic agents and their physiologic effects; and finally there is a summary discussion of the latest methods of anesthetic administration.

The principal editorial is concerned with the merits of periodic health examinations. The writer reflects that, "while it is frequently called a physical examination, the physical examination is the least fruitful though an especially necessary part of it. There are relatively few significant conditions that can be found on physical examination without having caused some indications that would be listed in careful history. The history, so often neglected, should be the foundation stone on which the remainder of the examination is built." The writer concludes: "It is common knowledge that really quite obvious findings will be missed unless something directs us to look quite specifically for them. An adequate history will frequently point a directing finger. Certain laboratory or x-ray work may be the solution of the problem, or perhaps some special examinations. There are so many of these that it is only by vigilant coordination of the facts found by the eyes, ears and fingers that the proper selection of procedure can be made. In this way patients can be saved from the dangers of neglect or the burden of excessive laboratory studies. We should always bear in mind that it is the things we don't think of rather than the things we don't know that cause the greatest woes in medicine.

Yet another editorial, "Tests by Number," comments on the rise of quantitation and statistical evaluation in medicine. "So far as medicine has risen from superstition to science, progress has been made over a way mapped by hard-gained experience, but the shortest road had always been found as a result of statistical examination of the phenomena which have been encountered along the way. Scientific medicine had its beginning with the statistical study of disease and its treatment, as introduced by Louis of Paris. He proved mathematically that venesection, the routine treatment of the time for pneumonia, not only was of no benefit but was distinctly injurious and responsible for many deaths. Holmes followed with his statistical study of puerperal fever, which shortly banished this curse from lying-in hospitals. Test by numbers is responsible for the use of the ligature rather than the cautery to staunch hemorrhage, for the prevention of small pox by vaccination, for the control of diphtheria by toxin-antitoxin. The list can be extended without end."

The Charles V. Chapin Hospital announces its internship staff which includes Drs Michael DiMaio, Walter Batchelder, Isadore Gershman, Corinne Eddy, and Harry Magnet.

Twenty Five Years Ago (January, 1965)

The lead article by Nathan Sonkin, MD, is entitled "Ice Water in the Ambulatory Treatment of Duodenal Ulcer." Prompted by Wangensteen's employment of gastric freezing for bleeding peptic ulcers and Palmer's use of ice-water lavage in the emergency treatment of upper gastrointestinal bleeding, the author treats a series of ten duodenal ulcer patients with an oral ice-water regime. The patients are instructed to drink at least one eight-ounce glass of ice water with each meal and between each meal. Two glasses are to be taken at bedtime. A control group of ulcer patients form the basis for comparison. The article concludes: "A new treatment method, the ingestion of ice water, has been suggested for the ambulatory office management of acute duodenal ulcer. It appears to offer a simple, economical method which does not present any problems in patient cooperation. It offers symptomatic relief rather quickly and hastens control of acute or recurrent duodenal ulcer. Further extensive experience is needed to evaluate its effectiveness and long-term effects. It is not suggested that this is a panacea for duodenal ulcer or that it should replace time-proven therapy. However, further trial with this safe and relatively simple measure appears to be merited."

Two cases of the malignant carcinoid syndrome, one treated by hepatic artery perfusion, are described by Drs Raymond Moffitt and Charles Jones.

Dr Alton Paull writes on recent advances in the diagnosis of pulmonary embolism and shows the diagnostic value of examining the serum concentrations of bilirubin, lactic dehydrogenase and

glutamic oxaloacetic transaminase, in distinguishing pulmonary embolism from myocardial infarction and pneumonitis.

A case report of obturator hernia of a loop of ileum resulting in almost total intestinal obstruction is described by Dr Warren Francis.

The *Journal* summarizes the actions of the AMA House of Delegates during the 18th Clinical Convention, Nov 29-Dec 2, 1964. With regard to human reproduction, the delegates adopt the following four-point statement: "1. An intelligent recognition of the problems that relate to human reproduction, including the need for population control, is more than a matter of responsible parenthood; it is a matter of responsible medical practice. 2. The medical profession should accept a major responsibility in matters related to human reproduction as they affect the total population and the individual family. 3. In discharging this responsibility, physicians must be prepared to provide counsel and guidance when the needs of their patients require it or refer patients to appropriate persons. 4. The AMA shall take the responsibility for disseminating information to physicians on all phases of human reproduction, including sexual behavior, by whatever means are appropriate."

A small news item notes that health insurance in 1953 covered 97 million Americans. "Since then there has been a coverage increase of more than 49% and a total of over 145 million persons were protected against the cost of hospital care at the year-end 1963. In 1953, 61% of the US civilian population were protected by some kind of health insurance, while at the beginning of 1963 77% were so insured."

The *Journal* notes the death, during the year of 1964, of many of its leading practitioners: L. Murray Beardsley, Edmund B. Curran, Halsey De Wolf, H. Lorenzo Emidy, Bernard F. Ferrara, Joseph C. Kent, Harold D. Kenyon, Louis I. Kramer, Frank I. Matteo, Henry F. McCusker, Edward G. Melvin, John E. Menzies, Joseph E. Murray, Amy E. Russell, Eliot A. Shaw.

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Necrology — 1989

Albert E. Geremia, MD

Doctor Albert E. Geremia, a cardiologist with an office in Providence for 40 years before retiring in 1975, died January 31, 1989 at the age of 85.

Doctor Geremia was a graduate of Tufts University Medical School in 1932. He studied electrocardiology in 1946 with Doctor Frank Wilson at the University of Michigan, Ann Arbor.

A World War II navy veteran, Doctor Geremia served as chief medical officer at St. Alban's Hospital, Long Island, NY. He was medical officer at St. Joseph Hospital's rheumatic heart clinic from 1948 to 1965, medical adjudicator for the Social Security Administration from 1959 to 1980, and staff consultant to Rhode Island Hospital since 1973.

Doctor Geremia was a member of the American Association of Internal Medicine, the Rhode Island Society of Internal Medicine and the Providence and Rhode Island Medical Societies. He was a former board member of the Rhode Island and New England Heart Associations and past president of the Malpighi Medical Society.

Doctor Geremia was the husband of Mary (LaCava) Geremia.

Frank Joseph Logler, MD

Doctor Frank Joseph Logler, surgeon, died February 15, 1989 at the age of 79.

Doctor Logler received a medical degree from Vanderbilt University in 1937.

He served two years in the Army Medical Corps in World War II at American bases in Argentina and Newfoundland where he was instrumental in setting up the base hospital. At the Lahey Clinic, he served a surgical fellowship.

Doctor Logler was senior surgeon at Newport Hospital and

courtesy surgeon at Rhode Island Hospital. He was a physician to the Virgin Islands government from 1975 to 1977.

Doctor Logler was professor at the Newport Hospital School of Nursing, Beverly Hospital School of Nursing and Salve Regina College. He was director of the Rhode Island Blue Cross Physician Service for eight years.

He was director of the Aquidneck Medical Associates, trustee of the Herbert and Daisy Stride Foundation for Medical Education, and the first president and one of three organizers of the Aquidneck Medical Association. He was a fellow of the American College of Surgeons, the International College of Surgeons, International Academy of Proctology and a diplomate of the American Board of Abdominal Surgeons.

Doctor Logler was a member of the Newport County and Rhode Island Medical Societies, the American Medical Association, Massachusetts Medical Society, Providence Surgical Society, New England Obstetrical and Gynecological Society, the Industrial Medical Association and the United States National Association of Medical Examiners.

He was a member of the State Peer Review Committee, the Rhode Island Medical Society House of Delegates and Medical Legal Committee.

Doctor Logler was the husband of the late Martha E. (Conway) Logler.

John C. Ham, MD

Doctor John C. Ham, internist, died March 4, 1989 at the age of 83.

Doctor Ham was a graduate of Harvard University Medical School in 1932. He joined the staff

of Rhode Island Hospital in 1936, where he was a consultant until his death. He was a consultant in internal medicine at Miriam Hospital, and also at Butler Hospital until 1981. Doctor Ham was a director of the Thoracic Clinic at Rhode Island Hospital from 1942 to 1966 and served on the staffs of Zambano Memorial Hospital, Veterans Administration Regional Medical Center and the former Charles V. Chapin Hospital.

Doctor Ham was past president of the American Thoracic Society, a member of the Providence and Rhode Island Medical Societies and the Providence Tuberculosis League. He was a board member of the Visiting Nurse Association, served on the board of the Rhode Island Lung Association, and was a member of the Friday Night Medical Club. Doctor Ham was a fellow of the American College of Physicians, diplomate of the American Board of Internal Medicine and a member of the American Medical Association.

Doctor Ham was the husband of Joan (Taylor) Ham.

Robert F. Rosin, MD

Doctor Robert F. Rosin, general physician in Pawtucket for over 30 years, died April 4, 1989 at the age of 73.

Doctor Rosin graduated from the University of Pennsylvania Medical School in 1942. He was a physician in the Army in World War II serving in the South Pacific Theater and in India and Burma.

He was a member of Pawtucket, Rhode Island and American Medical Associations.

Doctor Rosin was the husband of Devera (Grossman) Rosin.

Charles V. Cox, MD

Doctor Charles V. Cox, chief of anesthesiology at Memorial Hos-

pital from 1972 until retiring in 1986, died May 8, 1989 at the age of 68.

Doctor Cox received his medical degree from Ohio State Medical School in 1950. He was senior anesthesiologist at Rhode Island Hospital from 1954 until 1972, senior instructor of residents at Rhode Island Hospital from 1954 to 1973 and director of school of anesthesia for nurse anesthetists from 1973 to 1986. He was also clinical instructor in anesthesiology at Brown University from 1970 to 1986.

Doctor Cox was a member of the American Board of Anesthesiology, the American Medical Association, past president of the Rhode Island Society of Anesthesiologists, a member of the Rhode Island, Providence and Pawtucket Medical Societies, the AANA Council on Accreditation and the Honorary Physicians Society.

In 1962, he received an appreciation award from Medico for services rendered in Algeria during the Algerian Independence emergency. He received the Isaac B. Merriman Award for being a physician, healer and teacher.

Doctor Cox was the husband of Constance (Weldon) Cox.

James F. Hardiman, MD

Doctor James F. Hardiman, a practicing physician for 40 years before retiring in 1986, died May 10, 1989 at the age of 68.

Doctor Hardiman graduated from Tufts Medical School in 1945. He was on the staffs of St. Joseph Hospital and former president of the medical staffs.

He was a member of the American Medical Association, the Rhode Island and Providence Medical Societies, and past president of the Rhode Island Hemophilic Society.

Doctor Hardiman was the hus-

band of the late Margaret (Hogan) Hardiman.

Leo Stern, MD

Doctor Leo Stern, chief of pediatrics at Rhode Island Hospital, died May 17, 1989 at the age of 58.

Doctor Stern received his medical degree from the University of Manitoba in 1956. He was chairman of the pediatrics department at Brown University Medical School, member of the American Academy of Pediatrics, Royal Society of Medicine, Society for Pediatric Research, American Pediatric Society, Rhode Island and Providence Medical Societies, Canadian Medical Association, Canadian Pediatric Society, New York Academy of Science, Canadian Society of Clinical Investigation, Perinatal Research Society and the American Society of Clinical Pharmacology and Therapeutics.

Doctor Stern was the husband of Reva (Angel) Stern.

John H. Mulvany, MD

Doctor John H. Mulvany, a physician in Rhode Island for 60 years, died May 24, 1989 at the age of 83.

Doctor Mulvany received his medical degree from the University of London in 1927. He earned a number of specialty degrees at various London hospitals in surgery, internal medicine, pathology, neurology, obstetrics and gynecology. He attained the rank of lieutenant colonel in the Royal Army medical corps during World War II, at which time he was chief surgeon on the Queen Mary. He was on the staff of St. Joseph Hospital and Fogarty Hospital until retiring in 1987.

He was a Hunterian professor at the Royal College of Surgeons, member of the American and British Medical Associations, and the

Rhode Island and Pawtucket Medical Societies. He was a fellow of the College of Obstetricians and Gynecologists and a Fellow of the Royal College of Medicine.

Doctor Mulvany was the husband of Barbara (Gibbons) Mulvany.

George J. Dwyer, MD

Doctor George J. Dwyer, a physician in private practice for 42 years before retiring in 1976, died May 29, 1989 at the age of 85.

Doctor Dwyer graduated from Hahnemann Medical School in Philadelphia in 1932. He was a staff member of Roger Williams General Hospital throughout his career and became medical staff president in 1956. He was a member of the Rhode Island Medical Society.

Doctor Dwyer was the husband of the late Sarah (McGeough) Dwyer.

Palmer Congdon, MD

Doctor Palmer Congdon, a physician in Providence for 30 years, died June 13, 1989 at the age of 78.

Doctor Congdon was a 1936 graduate of Harvard Medical School. He worked for the US Department of Health in the then territory of Alaska from 1939 to 1941. He served as captain of the US Army Medical Corps evacuation team in the China-Burma-India Theater in World War II. Between 1974 and 1984, he was a supervising physician at Rhode Island Medical Center. He was a director of the personnel health clinic at Rhode Island Hospital for 40 years before retiring in 1986.

Doctor Congdon was a member of the Rhode Island Medical Society, Providence Medical and American Medical Association, and the Society of Internal Medicine.

Doctor Congdon was the hus-

band of Kathleen (Herbert) Congdon.

Frank A. Merlino, MD

Doctor Frank Merlino, practicing physician until retiring in 1980, died June 18, 1989 at the age of 86.

Doctor Merlino received his medical degree from the University of Maryland Medical School in 1928. He was executive secretary and medical director of the Providence Tuberculosis League for 20 years and medical director of the State Division of Tuberculosis Control for more than 35 years.

He was a member of the American Association of Chest Physicians, a member of the Rhode Island Medical Society and American Medical Association.

Doctor Merlino was the husband of the late Louise (Gregory) Merlino.

George E. Charon, MD

Doctor George E. Charon, general practitioner, died June 18, 1989 at the age of 76.

Doctor Charon graduated from the University of Montreal Medical School in 1944. He was a captain in the Army Medical Corps, serving the 4th Infantry Division in the Korean War.

He was a former president of the Rhode Island Chapter of the American Association of Family Practice, a member of the Rhode Island Medical Society and Providence Medical Association and served on the staffs of St. Joseph Hospital, Roger Williams General Hospital and Zambarano Memorial Hospital.

Doctor Charon was the husband of Noella (Raquier) Charon.

Merle M. Potter, MD

Doctor Merle M. Potter, general practitioner, died June 25, 1989 at the age of 97.

Doctor Potter received a med-

ical degree from Cornell University Medical School in 1917. She was the physician for girls in the Providence school system and physician for the former Pembroke College, now Brown University.

She was a member of the Rhode Island Medical Society and Providence Medical Association.

Whitman Merrill, MD

Doctor Whitman Merrill, a physician in private practice for 36 years in Coventry, died July 23, 1989 at the age of 84.

Doctor Merrill graduated from Tufts University Medical School in 1932. He enlisted in the Navy as a medical officer in World War II. He formerly served as town health officer for Coventry.

He was president and vice president of the Kent County Memorial Hospital staff and one of the incorporators of Kent County Memorial Hospital in 1951. He was a member of the American Medical Association and Rhode Island and Kent County Medical Societies.

Doctor Merrill was the husband of the late Gertrude (Wilkinson) Merrill.

Edward Damarjian, MD

Doctor Edward Damarjian, retired chief of anesthesiology at Memorial Hospital, died August 11, 1989 at the age of 79.

Doctor Damarjian graduated from Tufts Medical School in 1936. He started the school of anesthesia for graduate nurses at Memorial Hospital in 1965. He was instrumental in establishing an emergency cardiopulmonary resuscitation unit, known as "Cardiac 99." He was a captain in the Army Medical Corps during World War II and served with the 48th Evacuation Unit in the China-Burma-India Theater.

Doctor Damarjian was a member of the American Medical As-

sociation, Rhode Island Medical Society and Pawtucket Medical Association.

Doctor Damarjian was the husband of Shaki (Yorganjian) Damarjian.

Anthony C. Verrone, MD

Doctor Anthony C. Verrone, a physician in private practice, died August 21, 1989 at the age of 74.

Doctor Verrone graduated from Tufts University Medical School in 1941. He served in the Army Medical Corps in World War II. He had been an adjudicating officer for the Veterans Administration. He was also a staff member of St. Joseph Hospital.

He was a member of the Rhode Island Medical Society, Providence and American Medical Association, and the American College of Surgeons.

David K. Johnson, MD

Doctor David K. Johnson, a physician in private practice, died August 28, 1989 at the age of 35.

Doctor Johnson received his medical degree from the University of Iowa in 1980. He was certified by the American Board of Internal Medicine in 1983.

He was a member of the Rhode Island and Woonsocket Medical Societies.

Doctor Johnson was the husband of Laurie (Hilger) Johnson.

Jan S. Dudek, MD

Doctor Jan S. Dudek, a practicing physician in Johnston, died October 1989 at the age of 75.

Doctor Dudek graduated from the University of Lwow in 1939 and served as physician in the Polish Army in World War II. He was a graduate of the Royal College of Physicians in London, 1955. He was a member of the Rhode Island Medical Society and American Medical Association.

Doctor Dudek was the husband of Irena (Lopatniuk) Dudek.

Kieran W. Hennessey, MD

Doctor Kieran W. Hennessey, in private practice for 40 years, died November 1, 1989 at the age of 79.

Doctor Hennessey received his medical degree from Tufts Medical School in 1936. He served in the Medical Corps during World War II in the South Pacific and was awarded the Bronze Star. He was on the staff of Memorial Hospital for 40 years.

He was a member of the Rhode Island Medical Society and Pawtucket and American Medical Association.

Doctor Hennessey was the husband of Madelyn (Hoey) Hennessey.

Angelo R. Bologna, MD

Doctor Angelo R. Bologna, family physician, died November 19, 1989 at the age of 84.

Doctor Bologna graduated from Washington University Medical School in 1933. He also pursued a certified course in public health and occupational medicine at Bellevue Hospital Post Graduate School, New York, in 1961.

Doctor Bologna was a member of the American Medical Association, the New York State Medical Society, Queens County Medical Society, and Rhode Island and Providence Medical Associations. He was a charter fellow of the American Academy of Family Physicians, member of the American Occupational Medical Association, and a former member of the Industrial Medical Association. He served as an Army captain in WWII and performed surgery.

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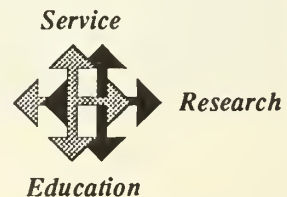
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Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

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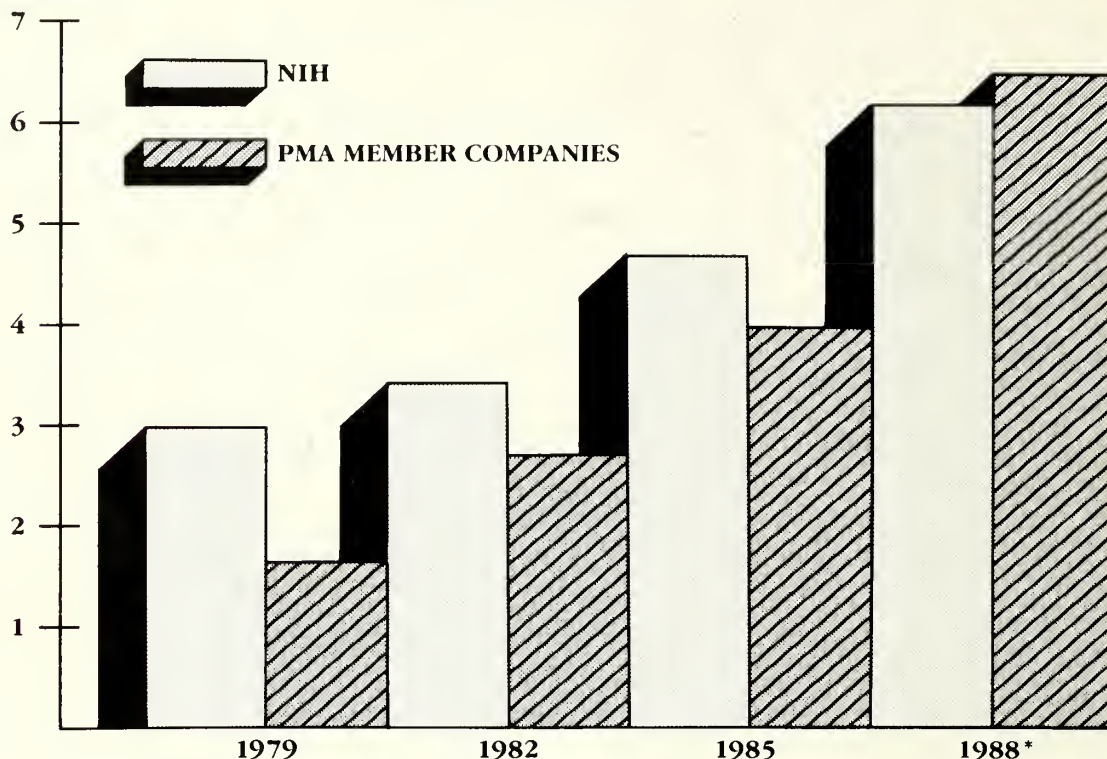
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Volume 73, Number 2 February 1990

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EDITORIALS

The Journal as a Forum for Unsettled Questions

The strength of a society rests to some measure upon its capacity to live with, tolerate and eventually confront unsettled, and unsettling, issues. When the tools of medicine had been limited to symptom-control and solicitude, its ethical problems were modest. However, as the science-fiction of yesterday merges into the reality of today, many new and vexatious questions inevitably arise.

Some of these contentious problems, such as the moral outrage evoked when blood transfusion or organ transplantation were first adopted, have abated with time; others have yet to be resolved. If any one of the new moral dilemmas facing medicine is to be resolved, the path must lie in continuing inquiry and earnest, open debate with minds not totally closed to the winds of change. It is therefore appropriate, indeed essential, that the pages of this *Journal* be employed in an airing of the tormenting questions which some of our technologic advances now generate.

It is the policy of this publication to encourage the presentation of controversial, conflicting views within its pages. The *Journal* welcomes responsible scientific and bioethical contributions as well as letters expressing the forthright, signed opinions of the Society's members. The *Rhode Island Medical Journal* speaks with many voices. With the passage of time, some may be proven valid while others eventually will best be forgotten.

This month's issue is devoted in part to the troubling moral uncertainties which accompany the recent observations that human fetal tissue offers substantial value in the treatment of a number of chronic human illnesses. Dr Eugene B. Brody, an imminent psychiatrist, bio-ethicist and currently Secretary-General of the World Federation for Mental Health, has provided the *Journal* with an international perspective on the medical use of fetal tissue. Brody's illuminating manuscript was submitted to two members of the clergy and two practicing physicians for commentary, and their responses are also printed herein. The readers are also invited to offer their opinions on this subject, and such letters will be printed in a subsequent issue of the *Journal*.

Stanley M. Aronson, MD

To Err is Human

It requires some courage to submit a scientific paper to a professional journal. A legitimate subject distilled from personal experience or inquiry needs to be identified; time must be dissected out of a busy schedule; writing skills must be recruited; and then the product of these disciplined efforts must pass the critical scrutiny of editors and readers. It is a daunting process, but fortunately for the survival of our

journals, there are sufficient numbers of busy people willing enough to undertake this perilous task of enlightening others with their original thoughts.

In emulating the accepted model of scientific writing, authors commonly dispense with eloquence and employ a lean, depersonalized style, emphasizing scientific content and reasoning. Statistical significance properly assumes more importance than syntactic elegance; and sometimes the excessive concerns over methodology and quantitation allow mere spelling errors to slip through undetected. Indeed, authors are terrible proof-readers of their own works, readily ignoring errors which are obvious to the more objective reader. One of the great truths of scientific authorship recognizes that typographical mistakes will be evident only after the manuscript is sealed and in the mail.

In reviewing manuscripts submitted for publication to this *Journal*, the editors encounter occasional spelling lapses. Most are banal mistakes in the category of *ie-ei* or *ible-able* confusions. A rare spelling error, however, imparts an unintended, and sometimes humorous, meaning to the sentence. In recent months, manuscripts submitted to the *Rhode Island Medical Journal* have included the following delightful typographic errors:
magnetic residence imaging
sacral ridiculopathy
rights of passage
symptoms wax and vein

I suppose that we should ac-

knowledge that there are operative, and perhaps etiologic, distinctions between mere inadvertent mistakes, gaffes, errors due to ignorance, paramnesias, parapraxes, and those special errors which arise from subconscious repressions, the Freudian slips. Some, perhaps all, of the specific errors cited above may represent the misinterpretations of a transcribing typist abetted by indifferent proofreading. Others may be Freudian — but they certainly do not achieve the world-class character of some such as the oft-quoted line from a college student's paper, "Freud's emphasis on sexuality is surely a phallacy."

We will continue to monitor the papers submitted to this *Journal*, primarily for their scientific content and merit; but when lapses of a more humorous kind materialize, we will share them with the readers so long as they do not identify the author. To err is human — and sometimes gently humorous.

Stanley M. Aronson, MD

The Rhode Island Medical Journal Heritage

In June of 1989 the *Journal* began a monthly column which summarized the contents of its issues of 25 and 50 years ago. We did this, and will continue to do so, in the belief that the legacy of our publication is an important part of our professional identity. Further, we stated that, "these short summaries will serve to demonstrate how far we have advanced in certain arenas, and how little we have progressed in others. Furthermore, the problems which seem novel to us today may reveal themselves to be problems which equally burdened our col-

leagues decades ago. It is also instructive to observe how the spectrum of diseases has evolved during these decades and the extent to which medical understanding has altered even our nomenclature. It is our hope that these synopses will be a source of both entertainment and education."

Some of the readers of this *Journal* have expressed pleasure in reading these distillations of our published past. For the editors the pleasure is even greater since we are obliged, at monthly intervals, to read two entire issues from the past in order to identify those segments worthy of republication. To read these older journals is to question constantly: "Did we really believe such things?" "How could we have reached such a bizarre conclusion?" "I thought that problem

arose only recently!" "What clinical wisdom — and without the aid of MRI!"

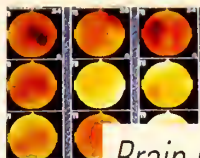
Ambrose Bierce once described history as an account mostly false, of events mostly unimportant, which are brought about by rulers mostly knaves, and soldiers mostly fools. We prefer to believe, rather, that there is much merit in reading the thoughts of the past. There is properly no history, said Emerson, only biography. Possibly so for society in general; certainly so for the profession of medicine. As a profession we are what we have accomplished as physicians working separately or together and the history of Rhode Island medicine represents nothing more and nothing less than the collective biographies of its many practitioners.

Stanley M. Aronson, MD

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Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it, however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

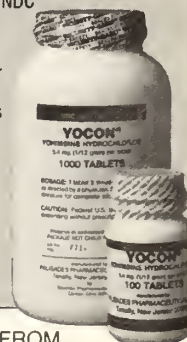
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon[®] 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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REAR VIEW



Women's Rights and the Medical Use of Fetal Tissue: An International Perspective

Eugene B. Brody, MD

... recent scientific discoveries and technological advances ... may ... endanger the rights and freedoms of individuals and will require continuing attention.

The Biomedical Technologies: Advocacy for Ethical Use

Contemporary medical preoccupation with the ethics of high-technology practice reflects two concurrent phenomena. One is the rise of health consumer organizations which act as advocates not only for patients but for all those who might some day require medical care; these are mainly active in the world's industrial democracies. The other is the nearly universal spread of advanced biomedical technology.¹ In developing nations, sometimes used to bolster an international image of health care progress, it co-exists with the folk healing and (often inadequate) primary care systems upon which the bulk of their populations depend.

The consumer movement gives

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educated patients a platform for health care advocacy as well as a stronger voice in medical decisions affecting their own futures. But biomedical science and its associated technologies (including such widely disparate approaches as non-invasive imaging, organ transplants, dialysis machines, endarterectomies, and neonatal survival devices) give physicians more effective clinical power than ever before. They command powerful means with unknown limitations, and unintended consequences (for patients, families and the broader community) which require deliberate scrutiny of the goals for which they are employed. High-technology medicine also increases the influence of the corporate profit-making entities which supply the technologies and the hospitals or governmental institutions which buy and service them.

These circumstances reinforce consumer advocate's concerns with maintaining the *autonomy* of individual help-seekers and their control over their own bodies. The Kantian principle of autonomy with its emphasis on equality of respect between persons has come to include patient and doctor. This principle, one of

the bases of the ideal of "informed consent," has also been viewed as encompassing the right of privacy applied to one's own body which is inherent in such earlier documents as the US Constitution.

The new technologies also reinforce the central position in health planning of the ethical principle of *justice*, in the sense of equal access to resources and equal freedom from harms or constraints; and of the principle of *beneficence*, in the sense that medical procedure should be intended for the primary benefit of the patient to whom it is applied rather than the community, the family or the medical profession. These principles are involved in deciding whether or not expensive biomedical technologies should be electively available only to privileged citizens, who can afford them, or part of entitled, publically supported, reparative medical treatment; whether they

ABBREVIATIONS USED:

IVF: *In vitro* fertilization

UN: United Nations

UNESCO: United Nations Educational, Scientific and Cultural Committee

should be developed and applied if it must be at the expense of basic health care and illness prevention for the bulk of a population; and whether the spin-offs and "trickle-down" effects of such development actually benefit the public health. The presumed rights to life, health and appropriate treatments of some members of the population must be balanced more sensitively than ever against the presumed rights of those whose taxes are expected to support or whose labor actually provides the requested resources. This complicated equation should also include the profit-making potential for those who manufacture, market or lease the necessary technologies, as well as the short and long-term health of the broader community, however measured. In this last framework fetal tissue transplantation is only one instance of the possible use of expensive, or rare, government or insurance supported, technology for the treatment of chronic disease.

Human Rights and Women's Rights in the Intergovernmental System

It is in this context that UNESCO's Division of Human Rights and Peace has revived an interest in the benefits and hazards of biomedical technology, including the possible use of fetal tissue for research or therapy. This general interest emerged in the first human rights instrument of the intergovernmental system, the Universal Declaration of Human Rights, adopted by the General Assembly of the United Nations at the beginning of the post-Nazi, post-World II era, on December 10, 1948.² The Declaration's health-related elements can be regarded, depending upon the observer's perspective, as entitlements or as freedoms. Thus, it af-

firmed rights to plan a family (Article 16), to basic health-related and social services (Article 25), and to share in scientific advancement and its benefits (Article 27). It also paid attention to gender equality stating that distinctions based on sex shall not interfere with the exercise of human "rights and freedoms" (Article 29). Its prohibitions of slavery, cruel treatment and arbitrary detention were elaborated in the 1966 International Covenant of Civil and Political Rights³ with its ban on inhumane and degrading treatment for detainees, including those in hospitals. More specifically it upheld the principle of due legal process in the deprivation of liberty under any circumstances including "detention on grounds of mental illness."

The 1948 assertion of a "right" to share in "scientific advancement and its benefits," basic to the now familiar question of equal access to scarce medical resources, was expanded to include freedom from the threats which science/technology might impose. Thus, in 1968, the International Conference on Human Rights⁴ warned that "recent scientific discoveries and technological advances . . . may . . . endanger the rights and freedoms of individuals and will require continuing attention." It recommended that UN agencies undertake a study of problems relating to human rights which arise from developments in science and technology. In 1969⁵ and 1979⁶ UN resolutions upheld free access to contraception and required member states to remove restrictions to access by unmarried persons, as well as rules requiring spousal authorization for such services, including sterilization and abortion.⁷ By 1985 the final report of the UN Decade of Women⁸ stated that "the ability of women to control their own fertility" is "an im-

portant basis for the enjoyment of other rights."

The autonomy advocated by these resolutions, reflecting the independence and achievement values of Western culture, does not fit the family and lineage oriented societies and the paternalistic traditions of the developing world. This was recognized by a 1985 conference of the International Social Science Council and UNESCO which noted that in applying the new advances in biology, "it is essential to ensure that the application decreases the economic and cultural disparities among social and national groups."⁹

. . . Women, in most of the world, are still in the position of a minority with inadequate access to the sources of societal power.

In practical terms the 1985 conference referred particularly to Third World peoples at risk of exploitation as test populations for biomedical products, or as secondary markets in which to "dump" products no longer in demand in more developed countries. But it was also aware of the possible use of mental hospital patients, the retarded or demented, prisoners, and even poor and uneducated paid "volunteers" as subjects for hazardous or unproved "treatments," albeit with their "consent." It is also recognized that one socially defined group which might be placed at risk by the new reproductive technologies, although it could also gain new opportunities from them, was the group of women. Women, in most of the world, are still in the position of a minority with inadequate access to the sources of societal power. Even in the industrial democracies such as the United States, those

women who are poor, migrant, refugee or ethnically different from the majority, and speak a different language from them, may be at particular risk from the new technologies. They have less access to health care; are at greater risk than others for illness, injury and chronic disability; and are at greater risk of being subject, without informed consent to potentially hazardous procedures.

Women's Rights and Fetal Tissue Use

Abortion: Fetal Rights Versus Maternal Rights. Most contemporary attention to fetal tissue use lies in its source: elective or spontaneous abortion or miscarried fetuses. Elective abortion is the central issue since spontaneous terminations of pregnancy often involve chromosomal aberrations or viral infestations which would make clinical use of the expelled tissue potentially dangerous and unethical. In terms of practical autonomy rights the aborted fetus has no personal voice; the pregnant woman who has produced the fetus, and elected to abort it, or her next of kin, are the only ones for whom such rights can be invoked. However, contemporary religious and political movements, fueled by medical research promoting a concept of the fetus independent of the woman of which it is a part, are recognized as threatening the rights of women and their freedom of autonomous action. They do so by asserting the primacy of the rights and interests of the fetus over those of the woman who has been an active participant in its conception, within whose body it grows, and upon whose welfare it is dependent for its own. Spallone declares that bio-science, itself, has limited the freedom of women by defining "the role and power of medicine"¹⁰ over them,

with special reference to the status of the fetus.

The rights problem typically emerges when the rights of the fetus are placed ahead of those of the pregnant woman. In some US cases non-consenting women have been forced by court order to undergo Caesarian section in order to save the life of the fetus. Others have been threatened with unprecedented restraint in order to prevent them from engaging in behavior considered dangerous to the health of the fetus. A recent survey¹¹ showed that 46 percent of heads of US fellowship programs in maternal-fetal medicine "thought that women who refused medical advice and thereby endangered the life of the fetus should be 'detained.'" Forty-seven percent supported court orders for procedures such as intrauterine transfusions" which invade the mother's body, without her consent for the presumed good of the fetus. The authors suggest that the targets of these interventions were in effect dehumanized and not treated in terms of the status granted them under the law. As evidence they note that 81 percent of women subjected to such court orders were Black, Asian or Hispanic; 44 percent were unmarried; and for 24 percent English was not the primary language. "The question" as they put it "is really whether doctors or the government may usurp patients' decision-making rights and appropriate or invade their bodies to advance what they perceive to be the therapeutic interests of a second patient, the fetus."

Property Rights Over the Fetus. Official commissions in every country which has issued statements about fetal tissue use (Australia, Sweden, France, the UK, Canada, the US), as well as the European Council, recommend insulating the woman's decision to abort from any decision about

the medical use of the fetal tissue. In effect they agree that the fetus constitutes a life independent of her own and that she does not have the right of choosing to sacrifice it for the possible benefit of another. They also agree on separating medical scientists who might do research on the issue from any decisions about the termination of pregnancy, including its timing and the method employed — which are clearly relevant to the developmental stage and potential therapeutic properties of the tissue. It is apparent that these representative appointed bodies, including physicians and scientists, suspect (across societies and cultures) that physicians' wishes to do research, to give their patients or friends the benefit of a new treatment, to be at the forefront of a social movement, to instill excitement into their practices, or other unidentified reasons, could lead them to engage in abortion-behavior which does not conform to the prevailing moral-religious-political-cultural codes of their countries. The intense US medical concern in this respect is revealed in the Stanford University Medical School Ethics Committee recommendation that the US Uniform Anatomical Gift Act which allows organ donations to specific persons for medical purposes be amended to prohibit designating a specific recipient for fetal tissue.¹²

The various governmental bodies do mandate the woman's approval for using the aborted fetal tissue for medical purposes. As Childress put it, the mother "still has a special connection with her fetus, and . . . a legitimate interest in its disposition and use. Furthermore, the dead fetus has no interests that the pregnant woman's donation would violate."¹³ These dicta seem to argue that, except for the *post hoc* consent,

after the abortion has been performed, a woman has no rights over the fetus which she has produced. As for economic rights the commercialization of fetal traffic is prohibited by all governmental commissions to date. Aside from general distaste for treating human tissue as a commodity the most widespread human rights concern is with the possibility that poor, minority or Third World women might come to consider the production and sale of fetuses as a legitimate occupation — an eventuality which would be considered by many observers as an instance of *de facto* exploitation of women rather than one of freedom of choice or of work. It has been suggested that producing a fetus for economic gain, or even to donate to a specifically designated relative or friend, would dehumanize the woman as well as the fetus. The anticipation of fetal production and sale, however, is based in part on precedent: the fact that bilateral organs, such as kidneys, have been sold, as have renewable body parts such as blood or sperm. It is also based on a perception of tissue sales as analogous to current exploitative economic practices throughout the world. These include hiring poor people to serve in hazardous occupations for pay, for example, volunteering as a paid soldier at risk of being exposed to combat; or the use of child labor which can inhibit the child's later development. As Robert Veatch of the Kennedy Center for Bioethics put it: "The same arguments that make it immoral to sell human organs seem also to make it immoral to fail to provide the necessities of life when they can be provided."¹⁴

The Justice Rights of Tissue Recipients. The argument is complicated by the presumed human right to "share in the benefits of scientific advancement," includ-

ing equal access to such benefits. Testimony from the National Coalition of Hispanic Health and Human Services Organization before the US Fetal Transplant Panel did not fully support the idea that the decision to abort should be insulated from that to utilize tissue. It noted that in the US Hispanic women have been 60 percent more likely than non-Hispanics to have an unintended pregnancy terminated by abortion (so that they could become intentional fetal tissue sources) and that they "suffer disproportionately from diabetes and AIDS — diseases where an effective treatment might be developed" from fetal transplant research.¹⁵ At the Fetal Transplant Panel hearings families of patients suffering from Parkinsonism lobbied vigorously for guidelines which would permit easy access to fetal tissue by those who might need it for therapeutic purposes. A more intense argument (Personal Communication) is exemplified in a statement from a female obstetrician in one of the European countries which has considered the matter. She said that if she had a child with juvenile diabetes she would consider if her right to become pregnant with the aim of aborting in order to obtain a fetal pancreas to implant into her child. Some ethicists suggest that, while many people might be repelled by the idea, this decision would not be inherently immoral: a fetus, while human, is not a person and, therefore, does not have rights. In contrast the doctor's diabetic child, already an emotionally invested and responsive figure in her life, is a person with rights, including a right to appropriate treatment. The mother, understandably, insists that her own rights as an adult member of society, a socially interactive, self-reflecting person acting as an independent moral agent, must take

precedence over those, if any, of her fetus.

Physicians as Ethical Interpreters and Technical Gatekeepers

In all of these transactions the physician is always the essential intermediary, the gatekeeper, between the woman and the would-be regulators of the production and use of fetal tissue. Some ethicists prefer the medical profession as monitor of how fetal tissue is to be obtained and used, to government control of reproductive behavior with the awful possibility of producing a new class of female reproductive criminals. At the same time the various commission reports, and a burgeoning medical literature on the subject, suggest that many physicians doubt their colleagues' consistent adherence to the principles of autonomy, justice and beneficence — even as the doubt coexists with respect for colleagues' conscious convictions.

... A female obstetrician ... said that if she had a child with juvenile diabetes she would consider it her right to become pregnant with the aim of aborting in order to obtain a fetal pancreas to implant into her child.

The ethical controversies surrounding fetal tissue transplants are colored by the continuing debate about other technologies influencing unborn humans. Many doctors feel the very availability of new technologies as a moral imperative for their use.¹⁶ This has been especially intense when dealing with infertility. Francois Laborie of the French National

Center for Health Research in Paris has noted with dismay the enormous expansion of so-called medical indications for in vitro fertilization (IVF) including the infertility of the male member of a couple.¹⁷ Even though exaggerated claims for the efficacy of IVF have been widely criticized the practitioner may be convinced of the high moral value of providing this service. It is difficult for patients and for many physicians to consider that a woman's best interest may not be served by a doctor's reinforcement of her desperate desire to become a mother at any cost. The doctor who accepts such "desperation" as normal, and justifying extreme measures to gratify it, may unwittingly be defending personal values or a set of cultural values that require re-examination.¹⁸ In any case the patient loses an opportunity, through counselling and guided introspection, to discover where her own best interest actually lies.

Conclusion

At present much of the argument about fetal transplant for therapy is premature. While the available data as to their clinical usefulness are promising, they are inconclusive. However, despite some reservations and obstacles, research on fetal physiology and the potential clinical value of fetal tissue has received more, cautious, approvals than disapprovals by national commissions. The history of medicine, and of other once problematic therapies which have been validated, suggests that if fetal tissue becomes established as an effective therapeutic agent, physicians will feel a moral imperative to provide it to their patients, just as they have with other new treatments. It seems unlikely that as more precise knowledge is gained of fetal developmental stages useful for

treatment purposes, and as methods for extracting fetal tissue without destroying organs become available, doctors will not determine the timing and methods of abortions in order to fit the medical use of the newly available fetal material.

Within the intergovernmental system, the UN, there is usually no pressure to translate human rights instruments immediately into action. Most can be understood as political compromises, ensuring the acceptability of involved Member States to the UN community while retaining sufficient ambiguity and generality to forestall domestic criticism. Those described above are an aspect of developing world culture in the technological era.¹⁹ Insofar as science/technology is the main driving force for cultural change these UN instruments facilitate such change. They constitute a gradually growing body of codified values acceptable to the educated leaders of most of the world's countries who recognize that their practical applicability varies with available resources.

... the physician is always the essential intermediary, the gatekeeper, between the woman and the would-be regulators of the production and the use of fetal tissue.

Aside from governments a key conduit of research-based ideas to world culture is the international corporate network. The biomedical research enterprise is central to the economies of the industrialized world, and uses the rest of the world as a market. As science/technology becomes, increasingly, a major basis for individual and group behavior in all of the world's populations their socially inherited, "traditional,"

values will be abandoned. The shape of those to come is still unclear. It is clear, however, that we are only at the beginning of some fundamental reconceptualizations of what is regarded as good, moral, correct, preferred or valued — and the reverse. Physicians, still the essential intermediaries who must apply the new technologies to help-seeking individuals, still vested by society with the privilege of invading the bodies and minds of fellow citizens, must be active, reflective participants in this process of culture change.

References

- Brody EB. Biomedical technology and women's rights. 1989; in *The Free Woman. Women's Health in the 1990s*. Eds E V van Hall, W Everaerd. Carnforth Lancs and Park Ridge New Jersey: Parthenon Publishing.
- United Nations. Universal Declaration of Human Rights. 1948; New York: United Nations. 1948.
- United Nations International Covenant on Civil and Political Rights. 1966; New York: United Nations.
- UNESCO. International Conference on Human Rights. Human Rights and Scientific and Technological Developments. Resolution XI. 1968; United Nations No. E. 68. XIV.2.
- United Nations. Resolution 1672 (LII). 1969; Social and Economic Council. New York: United States.
- United Nations. International Convention on the Elimination of Discrimination Against Women. 1979; New York: United Nations.
- Cook R, Haws J. The United Nations Convention on the Rights of Women: opportunities for family planning providers. 1986; *Internat. Fam. Planning Perspectives*. 2:49-53.
- United Nations. The Nairobi Forward-Looking Strategies for the Advancement of Women. Paragraph 29. 1985; New York: United Nations.
- UNESCO. International Symposium on the Effects on Human Rights of Recent Advances in Science and Technology. Organized by the International Social Science Council. Conclusions and Recommendations. 1985; Publication SHS-86/WS/39. Paris: Division of Human Rights.
- Spallone P. Beyond Conception. *The New Politics of Reproduction*. 1989; Granby Mass: Bergin and Garvey. p.157.
- Kolder V, Gallaher J, Parsons M. Court-ordered obstetrical interventions. *New Engl J Med*. 1987;316:1192-1196.
- Stanford University Medical Center Committee on Ethics. The ethical use of human fetal tissue in medicine. 1989; *New Engl J Med* 320:1093-1096.

- ¹³ Childress JF. Statement to the Advisory Committee to the Director NIH. Human Fetal Tissue Transplantation Research. Report of the Advisory Committee to the Director, NIH. 1988; Bethesda Maryland: National Institutes of Health. p. C7.
- ¹⁴ Veatch R. Death, Dying and the Biological Revolution. Our Last Quest for Responsibility. Revised Edition. 1989; New Haven and London: Yale University Press. pp. 292.
- ¹⁵ Human Fetal Tissue Transplantation Panel. Report of Consultants to the Advisory Committee to the Director, National Institutes of Health. 1988; Bethesda Maryland: National Institutes of Health.
- ¹⁶ Brody EB. New horizons for liaison psychiatry: biomedical technologies and human rights. 1989; Am J Psychiatry. 146:293-295.
- ¹⁷ Laborie F. Looking for mothers, you only find fetuses. 1987; in Made to Order. The Myth of Reproductive and Genetic Progress. Eds P Spallone and D L Steinberg. Oxford and New York: Pergamon Press. pp. 48-57.
- ¹⁸ Brody EB. Reproduction without sex — but with the doctor. 1987; Law, Medicine and Health Care. 15:152-155.
- ¹⁹ Brody EB. Culture, reproductive technology and women's rights: an intergovernmental perspective. 1988; J Psychosom Ob and Gyn 9:199-205.

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Four Commentaries on the Brody Paper

The excellent paper by Dr EB Brody on women's rights and the medical use of fetal tissue, written expressly for the Rhode Island Medical Journal, addresses problems and raises questions which the medical profession cannot avoid. The editors have requested that knowledgeable members of the Rhode Island medical and theologic communities provide the Journal with brief commentaries on those critical issues raised by Brody; their varied opinions are published below.

In Response to the Use of Fetal Tissue

The Reverend David Shire

This response to Dr Brody's paper is based on the conviction that those of us concerned with religion and ethics need to participate in these discussions. As a parish minister involved in statewide health care decisions, it is a privilege to be asked to share in this process.

The Gatekeepers

I commend Dr Brody's concluding statement that "physicians must be active, reflective participants" in the ethical discussion regarding the use of fetal tissue. So, too, must be clergy and the regulatory agencies of government, as well as what Dr Brody calls the "consumer movement" and the "educated patients." All of us together must be the gatekeepers. And although he states that much of the argument about fetal transplant is premature, eth-

ical debate can never be premature.

The paper demonstrates clearly that no longer is the medical profession educating physicians with only technical and scientific training. The study of ethics, and a deeper awareness of the patient as the consumer of medical services who shares in the decisions regarding his or her own health care, should remind us all that this recent theme in medical education must be continued and significantly expanded. The same must be true for those of us whose primary concern is the pastoral ministry. We must extend our knowledge into the current issues of health care and the complex ethical issues which surround them.

Some Theological Foundations

The United Church of Christ's "Pronouncement on the Church and Genetic Engineering" (General Synod XVII 1989) provides theistic guidelines for our discussion on fetal tissue research.

"God creates through the process of nature. As we discover these processes and learn how to use them, we find new ways to exercise covenantal responsibility with God in the on-going creative and redemptive work." A covenant is an agreement wherein both parties commit to provide specific things. God commits to provide us with insight into God's

will for us and with the ability to discover and grow. We, in turn, commit to use that knowledge in ways consistent with the highest and best we know. I would adapt another concept offered in the denominational pronouncement on genetic engineering to include fetal tissue research: "Genetic engineering (fetal tissue research) may give us new ways to relieve suffering. Certainly we must be concerned about and guard against injustice, misuse and undue risks, but we believe the greater immorality would be for the church to stifle or ignore (fetal tissue research's) promise for human benefit."

Covenant and Justice

With new knowledge comes new responsibility. These new responsibilities grow out of our Judeo-Christian concepts of covenant and justice. God's part of this covenant is forged with the realization that God is the Giver of life and knowledge. Our part of the covenant is the responsibility to use all knowledge for the betterment of humankind, not merely "to do no harm" but to intentionally try to do good. Despite a fundamental respect for all life, including embryonic life, we are constantly challenged to weigh one good against another: the mother's right to reproductive freedom (UN report), and the right of living persons to new technol-

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ogy and those discoveries that cure disease, against the "rights" if any, of a fetus. The lack of consensus regarding abortion and the pressure from segments of the religious community to involve government in enacting restrictive legislation which limits a woman's right to reproductive freedom, should not inhibit a covenant being shaped between those parties who would work ethically toward discovering new ways of healing disease. An inappropriate covenant in a pluralistic society would be one shaped by a particular viewpoint and then legislated to affect all persons. Those women who choose not to exercise their right to an abortion should always have that right, but the rights of others should not be abridged. Our concept of justice would then be fulfilled and fetal tissue, in this instance, would be made available for research under guidelines that support the researchers' need to discover, the rights of women, and the right of the sick to be healed.

Dr Brody demonstrates that many have been working to establish just guidelines, ie, the UNESCO symposium referenced in his footnote #9, the Stanford Medical Center Committee on Ethics in his footnote #12, and the report from the panel of NIH. Such responsible efforts would work toward safeguarding the research and researchers from committing the abuses of which we can presently conceive; especially the making of profit at the expense of minority women in developed countries, and all people in developing nations, including those upon whom experiments might be performed. These guidelines must include the right of each woman to decide whether or not her fetus may be used in medical research. Such guidelines would respond to the politically motivated ban that Health

and Human Services has placed on fetal research and would help remove the politics of abortion rights from this discussion.

Profit and Access

Dr Brody's reference to the international biomedical enterprise and its importance to the economics of the industrialized world needs response here. Aware as I am of the motivation and benefits of profit in our economy, there is an argument to be made for the ban of all profit from scientific research that would have therapeutic possibilities. The commercialization of the health care system and its technology tends to work contrary to the concept of justice. We need to ask if justice would better be served were we to channel research through non-profit and government-funded programs. Access to all scientific advances in health care

is the right of every human being, especially those who lack societal power, whether in developed or developing nations. These persons should be served by those of us who control the research. This is the true meaning of justice and of ministering to the common good. Anything else is exploitation. This concept would help respond to concerns regarding access and the high cost of transplanting fetal tissue in persons with diabetes or Parkinson's disease, if indeed the concept ever does prove therapeutic or curative.

We in science and religion are joint stewards of the God-given resources which surround us. Let us continue the dialogue that will help implement the United Nations Universal Declaration of Human Rights.

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The Fetal Tissue Issue

Reverend Albert S. Moraczewski, OP, PhD

Acrimonious debate has arisen between those who favor the use of electively aborted fetal tissue transplants for treating certain serious diseases such as Parkinson's and Alzheimer's and those who oppose such use. Both sides are convinced that their respective position is the one which is morally correct. Each looks on the other position as lacking moral probity and humane sensitivity. Each is vociferously indignant at the intransigent stance of the other.

Such a polarity makes rational discussion of the differences and the formulation of public policy all the more difficult. Yet clarification and working resolution need to be formulated. But how? Perhaps the first step in that direction is to identify the points of agreement and disagreement as a platform for discussion. Then, based on a common understanding, the second step would be to seek to formulate a policy which recognizes and respects the differences without compromising, however, the basic rights of fetus and mother.

Points of Agreement

I believe both groups agree that it is good to cure the sick, to alleviate pain and suffering, and to reduce as much as possible the handicapping effects of a dis-

ease. Both groups would also agree, I believe, that one should not directly and seriously harm some persons in order to help others. In addition, there is agreement, too, in respecting the need for appropriate consent whenever a human being is the subject of research or treatment. Other points of general agreement are that medical resources should not be wasted and that an individual conscience would be respected as long as it does not violate basic rights of others.

Points of Disagreement

The principal area of disagreement is the abortion issue as it relates to the use of fetal tissues. Those in favor of induced abortion admit generally that while abortion is not desirable in itself, it can be tolerated. It is morally and legally acceptable because it avoids greater problems for individuals, families, and society. Furthermore, those who accept elective abortions point out that the human embryo or fetus, while members of our species, are not yet human persons and do not have basic moral rights, including the right to life, associated with a born human child. They add that the rights of an actual living person, ie, the mother, should not be overshadowed by a being who is only a potential person.

A contrary rationale is held by those who oppose abortion. Abortion is a national disgrace involving the deliberate killing of about 1,500,000 unborn human persons each year (about 4,000 per day) in the United States alone. Those who consider in-

duced abortion to be morally evil hold that from conception onwards the fetus must be treated as a human person, albeit a very young person, who has nonetheless an inherent basic right to life. Consequently, any use of electively aborted fetuses, or their tissue, must also evaluate such use in light of the abortion issue.

The Medical Use of Fetal Tissue

The different attitudes towards abortion and opinions regarding the status of the very early human embryo are the bases for the opposing views toward the use of fetal tissue. Those in favor of using fetal tissue for medical research and treatment argue somewhat in the following (See, George J. Annas and Sherman Elias, "The Politics of Transplantation of Human Fetal Tissue," *New England Journal of Medicine*, April 20, 1989, pp.1079, and "Ethical Use of Human Fetal Tissue in Medicine," H.T. Greely, et al, op. cit., pp.1093-1096). Not to use aborted fetal tissue for research which would save many lives or restore health and function for numerous persons with disabling diseases would be unethical. It would be a terrible waste of a valuable resource. Furthermore, it is not evident, they hold, that the use of such aborted fetal tissue actually would encourage more women to have abortions. To reduce that unlikely possibility, care would be taken by the transplantation team that informed consent for the transplantation of the tissue would be sought after a decision for abortion had already been made by the woman or couple. Without the

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availability of fetal tissue from brain or from other fetal organs, it is asserted, medical research will suffer a notable set-back. The acquisition of new basic knowledge will be hampered and advances in new therapeutic modalities will be delayed or prevented. The plight of those with such debilitating diseases as Parkinson's or Alzheimer's is so severe that any avenue which affords hope should be pursued.

Opposition to Medical Use of Fetal Tissue

Those who oppose the use of fetal tissue from electively aborted fetuses argue according to the following rationale. In itself, that is, abstracting from the circumstances of a particular case and the sources of the tissue, the transplantation of human fetal tissue to relieve in another person a pathological condition for which currently there are no other morally acceptable and scientifically feasible means, under the proper conditions, can be morally acceptable. But to use tissue from deliberately aborted fetuses is morally problematic because it is making use of tissue obtained from what objectively is a morally evil act.

It is asserted by those who support fetal tissue transplants that precautions would be taken so that the woman's abortion decision is made independently of and prior to the decision for transplantation. However, with the increasing publicity of the potentialities of fetal tissue transplants, a greater number of women (and couples) may be swayed to have an abortion by the "reassuring" thought that some good will emerge from what was otherwise for them a catastrophic situation.

Murder and Use of Tissues

It has been argued (Daniel P. Sulmasy, "By Whose Authority?

Emerging Issues in Medical Ethics," *Theological Studies*, March, 1989, p.102) that since it is morally acceptable to use tissue from a murdered adult person, then it should be acceptable to use tissue from an electively aborted ("murdered") preborn child. The argument is not convincing because, the parallel, I believe, does not hold: 1) The one who slays unjustly another person, is considered by law as a murderer and is legally a criminal. This is not so in the case of an aborted child; the civil law does not consider either the woman or the physician performing the abortion as criminals. 2) Furthermore, murder is not a medical "industry," whereas abortion is and is economically beneficial for the medical "team." (Granted that the "hired gun" may make money on a contract to "terminate" someone, the majority of murderers are not of this type.) 3) In addition, abortion involves the most vulnerable and defenseless group of human beings. Anything which would place that group at even greater danger should be vigorously opposed. There is much closer connection between abortion and the medical use of fetal tissue than there is between random murders and the medical profession's use of cadaveric tissue from such a source since abortions are generally performed by physicians.

Consequently, for the above reasons, one cannot persuasively argue for the moral use of fetal tissue from electively aborted preborn infants on the basis that the use of tissues and organs from a murdered person is morally acceptable.

Less Motivation for Alternate Sources

Another reason for opposing the use of fetal tissues from induced abortions for medical and re-

search purposes is that the ready access of such material is likely to lessen the effort to search for alternative treatment for such disorders. Funding from government and private sources are not likely to be forthcoming if there is a general public impression that tissue from aborted fetuses is plentiful, meets medical and research requirements, and is morally acceptable.

The proposal of the Human Fetal Tissue Transplantation Research Panel (National Institute of Health, 1988) that the abortion team should be distinct from the transplantation team is seen as an exercise in futility. To assert that stringent steps will be taken to avert commercialization of such tissues is a tenuous claim; to say that the abortion decision will be made independently of any consideration of transplantation is inadequate assurance. To say that, if we do not formulate some laws to regulate the process, the use of aborted fetal tissue nonetheless will proceed in non-government funded projects and in foreign countries, is certainly not convincing (see, *Science* 23:December 1988, pp.1625-6).

Possible Alternative Approaches

If the tissue were to be obtained from spontaneously "aborted fetuses" that is, from miscarriages, there would be little moral objection on that score since the fetus was not "evicted" by free, human intervention. While in itself the loss of life is a physical evil, it is not a moral evil. In the case of tissue obtained from such fetuses the issue of free, informed consent would be dominant. With appropriate consent and due respect being paid to the fetal cadaver, such tissue could be utilized for medical research and the treatment of human diseases.

Using tissue from sponta-

neously aborted fetuses, however, has limitations. This resource is unreliable because miscarriages often happen in circumstances not suitable for subsequent tissue transplantation. Furthermore, spontaneous abortions often occur because the individual conceived has serious genetic defects. The problem of obtaining informed consent from distraught, bereaved parents in a timely manner is a sensitive one. And there are insufficient numbers of fetuses in a suitable stage of development and condition.

To solve some of these difficulties, it has been suggested that cell-culture procedures may be another resource for tissue transplantation. Such cells would have been genetically altered to function as the specific cells a patient is lacking (see Leslie Bond, "Promising Alternatives to Fetal Tissue Use to Patients," *National*

Right to Life News January 22, 1989, p 9, 12). No doubt at this time such alternatives are still in the early stages of development. Yet research on these will be pushed less rigorously if electively aborted fetal tissues are, or become, readily available. Adequate research funds will not be forthcoming if the need appears to be met by present technology.

Tragic as the plight of persons with Alzheimer's disease, Parkinson's disease, diabetes and other serious disorders potentially treatable with fetal transplant tissue may be, compassion for them cannot justify the use of a morally evil means to cure or ameliorate their condition. The director of the National Conference of Catholic Bishops office for Pro-Life activities has supported an earlier White House proposal (of the Reagan administration) "of an executive order forbidding federal

support for experimental transplants using organs and tissues from abortion victims" (Fr John Gouldrick, CM, "Aborted Fetal Tissue in Experimental Transplants Opposed," *Origins*, Jan 5, 1989, 495-6). What the present administration under the leadership of President George Bush will do with this "tissue issue" remains to be seen.

Even with the differences of moral positions held by medical researchers, practicing physicians, theologians, ethicists, members of Congress and of the administration, it should be possible to contribute to the well-being of patients with these various disorders without doing so at the expense of the most vulnerable members of our society — the unborn human infant.

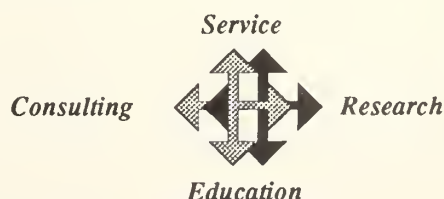
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Concerning the Use of Fetal Tissue

Boyd P. King, MD

I recently had the following conversation with a prominent obstetrician. I asked him to define, from a strictly scientific point of view, when an individual's life begins. Appearing bemused at the naivety of my question, he replied that he had no idea of the answer. I asserted that it must begin no earlier than the moment of conception and no later than the moment of birth. He replied, "Maybe, but if you first could tell me what life actually is, I might be able to define when it begins." When a third party barged in with the suggestion that the essence of life resides in the X-chromosome, the subject of discussion was abruptly changed to a less controversial topic.

This anecdote, although superficially amusing, may serve as an illustration of the scientific and ethical morass into which we have fallen when considering issues raised by the treatment of products of conception. As exemplified by the conversation, there is no general consensus regarding the basic definitions of the nature of life, when it begins, or what to do regarding the more specific issues of abortion and the medical use of fetal tissue. The rapid pace of scientific progress and the changing nature of social thinking have outstripped our culture's ability to absorb them into a coherent philosophical and ethical

framework with which we can generally agree. The guidelines provided by traditional teaching are strained to the breaking point, having never dealt with issues that raise questions that are unique and without precedent. Nevertheless, our society must come to some agreement regarding products of conception, for to blunder on into the future without one would be treacherous. Unfortunately, nothing approaching such a consensus seems imminent.

The issue of abortion, closely allied to the use of fetal tissue, is an illustration of the perils of existing without an agreed-upon system of values. Currently in the US, about one-third of conceptions are aborted. This epochal change in the way our society chooses to constitute itself is defined by some as a form of random genocide and by others as the expression of the woman's legitimate right to determine the fate of the fetal tissue for which she serves as host. The view of most people is hard to ascertain, since the expediencies surrounding the decision to abort usually overwhelm the relatively abstract ethical considerations. One is suspicious that many people believe that the fetus is alive, for this accords with traditional thinking, but that, under certain circumstances, abortion is appropriate. These ethical considerations raise uncomfortable questions which are usually avoided; better to get on with the abortion. This approach, acceptable for many individuals, is inadequate for society at large, which is being forced to deal with scientific advances which are even more difficult.

The article by Brody attempts to raise the level of consciousness regarding the issues surrounding the use of fetal tissue and to steer the reader through a maze of political, and legal issues. As such, it may serve as an illustration of the pitfalls of proceeding into the brave new world of evolving technologies without agreement on basic definitions. After a brisk review of the historic principles of autonomy and justice as they relate to recent developments in consumerism and technology, the author takes up the issue of women's rights. Proceeding from the UN's pronouncements regarding human rights starting in 1948, Dr Brody vigorously asserts the values systems he associates with the presumably advanced West as opposed to those that are "family and lineage oriented" and associated with the "paternalistic traditions of the developing world." In doing so, the author errs twice in assuming both that Western society uniformly accepts the decidedly liberal policies of the UN and human rights movements, and that these value systems, even if agreed on by the West, are superior to those of the "developing" Third World. This chauvinistic attitude repeats the errors of countless evangelicals who strode into distant regions to show the rustics the ignorance of their ways. Based on the collective behavior of the West this century, it would be difficult to persuade a citizen of the Third World that our contemporary view on rights and society are superior.

The discussion of woman's rights and the use of fetal tissue, mainly because of our cultural

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lack of consensus regarding the issues raised earlier, gets into some exquisitely illogical difficulties. Without trying to parse out the inconsistencies, it is apparent that an argument that maintains the fundamental right of women to have an abortion will have difficulty coexisting with the idea of the fetus as an independent human being. Yet the author sides with multiple commissions studying this issue that maintain "the fetus constitutes a life independent of" the mother. If this doesn't mean that the fetus is alive and human, what does it mean? If, in fact, the fetus is alive it must be protected and cannot be sacrificed prospectively, except to protect the life of the mother. If it is simply a mass of tissue existing at the behest of the mother, then the evolving thinking that surrounds such areas as organ donation, as well as established patient care precepts, should suffice. These

are intriguing questions that no one, be they ethicist, political scientist, or physician, has been able to discuss consistently. Nevertheless, the author puts the issues surrounding fetal use before us, and the logical dilemmas that emerge have as much to do with the intractable subject matter as with the views of the author.

The medical use of fetal tissue, like abortion, is here to stay and doubtless will find increasing applications that will benefit countless people in the future. Patients have a right of access to these developments and women have a corresponding right to control their bodies. The fetus, depending on one's definition, may or may not have rights. To this reader, this is the key question that, despite the juggernauts of recent social thinking and scientific progress, still eludes a firm answer. Physicians as "essential intermediaries" when dealing with

the products of conception, whether it be abortion or the medical use of fetal tissue, must decide whether they can afford to go on regarding such issues as strict medical questions to be decided within the context of the physician-patient relationship, or whether they will address the perplexing underlying issues that await rational explication. Dr Brody draws our attention to all these issues and firmly places the medical questions within the broader social and political milieu. Rhode Island physicians, whether or not they agree with all the positions that are staked out in the discussion, should now be more aware of the issues they must face. The issue of abortion awaits us in the Rhode Island legislature this spring; can questions and legislation regarding "fetal use" be far behind?

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The Feminine Approach in Ethics and Medical Decision-Making

Marsha Duke Fretwell, MD

The paper "Women's Rights and the Medical Use of Fetal Tissue" by E.B. Brody presents the argument that application of research using fetal tissue for the treatment of a variety of chronic illnesses will lead poor women and their obstetricians to a commercialization of their respective abortion behavior. That is, poor women in both the United States and in undeveloped countries will, for remuneration, increase the numbers of pregnancies directed toward abortion and some physicians will begin to offer fetal tissues as a routine therapy as others modify the timing and methods of abortion in order to fit the medical uses of the material. In this paper, Brody has used the masculine or "rights and justice" approach to ethics in a situation that is profoundly feminine and, in doing so, may misrepresent the behavior of the women and their doctors. I agree with the principle that economic incentives are powerful, but find that another ethical approach, the feminine or "responsibility and relationship" approach, may offer a more optimistic and useful analysis of the behavior of both the women and physicians in this complex situation.

Dr Brody examines the poten-

tial impact that the medical use of fetal tissue might have on individuals in the United States and in developing nations who are eager to participate in the economic boons of medical technology. He first discusses maternal rights versus fetal rights versus property rights of the fetus. Using the experiences of unmarried, non-English speaking, poor, Black, Asian and Hispanic women in the United States whose decision-making rights were usurped by court orders for the purpose of protecting their fetuses, he demonstrates the vulnerability of women throughout the world who have not achieved autonomy and are therefore at particular risk of exploitation. Although the commercialization of fetal tissue traffic is prohibited by all governmental commissions to date, he raises the possibility that poor, minority or Third World women might consider the production and sale of fetuses as a legitimate occupation. He then discusses the potential conflict of maternal rights, fetal rights and justice rights of tissue recipients, using the situation of a female obstetrician who said she would consider getting pregnant with the aim of abortion for the purpose of obtaining fetal tissue to treat the chronic disease of her living child.

Responding to this argument, I turn to the work of Carol Gilligan which examines actual interviews of women who were making decisions about undergoing abortions. In her book, *(In a Different Voice*, Harvard University Press, 1982) she begins with the concept that the "essence of

moral decision is the exercise of choice and the willingness to accept responsibility for that choice" and acknowledges that, until recently and perhaps not even yet in developing countries, women have not always had that freedom of choice.¹

From the interviews with these women a moral language distinct from that of men emerges and she then traces a sequence of development. Quoting Ms Gilligan: "women's construction of the moral problem as a problem of care and responsibility in relationships rather than as one of rights and rules ties the development of their moral thinking to changes in their understanding of responsibility and relationships, just as the conception of morality as justice ties development to the logic of equality and reciprocity." Initially, the focus of the woman is on caring for herself in order to endure survival. This is followed by a transitional phase where this is felt to be selfish and the woman develops a new understanding of self, other, connection and responsibility. The second focus in development is a maternal morality that seeks to care for the dependent, at all costs. If she does this without considering herself in the caretaking equation, another transition is initiated and leads to the third phase. This phase is marked by an increasing differentiation of self and other, an understanding of human relationships and the choice of care as opposed to injury as the ethic underlying her decision-making.

How does this "relationship

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and responsibility" approach to decision-making alter the analysis presented by Dr Brody? First, it allows us to see the increasing autonomy of women in decision-making about abortion not as the beginning of the breakdown of traditional values, but as the first step to freedom of choice and increased responsibility in decision-making for women. Secondly, it clarifies the critical role of family and societal support in the lives of maturing women because it allows them to move beyond the first or "survival" phase of decision-making about abortions.

Thus the "fundamental reconceptualization of what is regarded as good, moral . . ." in Dr Brody's conclusion may only be the reconceptualization required to include both feminine and masculine modes of social experience and interpretation into the everyday reality of life. The most important change in the analysis appears as we reexamine the situation of the mother considering an abortion for obtaining fetal tissue to save the life of her living child. Gilligan's work suggests that the concept of "rights" do not play a significant role as most women approach this type of decision. Rather, the relationship with her chronically ill child and its father and her ability to provide care in this, a potentially powerful fashion, would form the structure of the decision. The conflict would not be between the rights of the various participants involved but would be within the mother concerning her responsibilities to her live child and the fetus.

The discussion in this paper describing the behaviors of physicians as ethical interpreters and gatekeepers raises some issues about the difficulties physicians may have with patients and economic incentives pushing them

to the use of new technologies. In addition to the separation of the medical scientists who might do research on the issue from any decisions about termination of the pregnancy, it is important to consider what types of patient-doctor relationships might facilitate ethical decision-making about the use of this type of technology. Parallel to our discussion about the relational nature of ethical decision-making in women, it is likely that those patient-doctor interchanges based in a connectional or transpersonal dimension of human relationships are the most appropriate. This concept of the therapeutic doctor-patient relationship as connectional is described by Suchman and Matthews.² Showing how an illness may threaten a patient's sense of connection to others and the world, they describe how "a feeling of connectedness with the doctor, of being deeply heard and understood reduces this feeling of isolation and despair." It is in this relationship that a physician opens herself to increased responsibility or, to use the words of Gilligan, opens herself to responsible caring. Because the connectional experience is not the same as an emotional attachment, it may be the optimal relationship for assisting and supporting patients in the task of responsible decision-making.

Is this the type of relationship that we should offer our patients? As an internist who has a special interest in the care of frail, very old patients, my direct experience is in supporting patient's decision-making about dying, not abortion. The irony of the approaching medical use of fetal tissues for the treatment of the chronic illnesses of aging is in its completion of the circle of human development. In doing this, it clearly demonstrates the connections among all of us.

References

- ¹ Gilligan C. *In a Different Voice: The Psychological Theory and Women's Development*. Harvard University Press, Cambridge, Massachusetts, and London, England, 1982.
- ² Suchman AL, Matthews DA. What Makes the Patient-Doctor Relationship Therapeutic? Exploring the Connexional Dimension of Medical Care. *Ann of Int Med*, 1988;108:125-130.

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Primary Movement Disorders

Joseph H. Friedman, MD

The emergence of a subspecialty of neurology focussing on disorders of movement is a recent phenomenon that reflects in part the greater specialization of academic clinicians but more importantly reflects increased knowledge and ability to treat these illnesses.

"The neurologist of popular myth resembles a war correspondent with a slightly unhealthy interest in uncontrollable catastrophes."¹

The above statement describes what many physicians and medical students think of neurology. They believe it is a diagnostic field populated by therapeutic nihilists. While it is true that neurology is largely a diagnostic discipline, it is also committed to treatment. The developing field of movement disorders is a good example of this. Unlike most medical specialties, in movement disorders as in dermatology, "what you see is what you get." While this isn't completely true, in that some rare movement disorders are episodic and hence may not be visible in the doctor's office, almost all movement disorders and the

problems they cause are visually evident to the physician. This allows the physician both to interpret complaints accurately and to evaluate therapy.

The emergence of a subspecialty of neurology focussing on disorders of movement is a recent phenomenon that reflects in part the greater specialization of academic clinicians but more importantly reflects increased knowledge and ability to treat these illnesses. Most disorders of movement can be treated to some degree, with the general rules being: (1) treatment is symptomatic so that medications should be used only if they work; and (2) before abandoning a drug, push it slowly (and safely) to mild toxicity before declaring it unhelpful.

Most movement disorders specialists are very aggressive in their approach to the treatment of movement disorders and will try multiple medications to improve a patient's control of his own movements.

There are several ways of categorizing movement disorders. One can look at etiology and divide the field into the naturally

occurring and the iatrogenic disorders, the latter being more common. Only naturally occurring disorders will be considered here. Naturally occurring disorders are characterized by their phenomenology and can be classified into disorders of excess movements or too few movements. Both frequently involve disordered movements as well. The overlap is large so that many patients fall into both groups.

Akinetic Rigid Syndromes

The akinetic rigid syndromes are the parkinsonian ones. Parkinson's disease (PD) is the paradigm for this collection of disorders and is the most common. PD affects about one percent of white Americans above the age of 65 years and probably occurs less frequently in other ethnic groups.

ABBREVIATIONS USED:

GTS: Gilles de la Tourette syndrome

NPH: Normal pressure hydrocephalus

PD: Parkinson's disease

PSP: Progressive Supranuclear Palsy

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However, about 15 percent of people diagnosed as having PD turn out to have other illnesses.² The most common misdiagnoses are essential tremor, progressive supranuclear palsy (PSP) and striato-nigral degeneration.

Progressive Supranuclear Palsy

Progressive Supranuclear Palsy (PSP) occurs in about five percent of people diagnosed as having PD.² For such a relatively common disorder with such a distinctive appearance it is surprising that it was not recognized until 1964.³ Early in its course it appears to be typical PD except for the absence of a resting tremor. Since 20 percent of PD patients lack a resting tremor the absence of one is therefore not diagnostic. The lack of a good response to L-DOPA, typical of PSP and atypical of PD, is much more helpful. After a few years PSP clearly takes a course distinctive from PD. Axial rigidity occurs, with the neck and back usually arched backwards. This is accompanied by an increasing problem with postural instability and a tendency to fall backwards. The face takes on a fixed, quizical look due to facial dystonia and the voice changes, with a slow pressured dystonic speech. Loss of voluntary, vertical eye movements is the sine qua non for the diagnosis of PSP but patients manifest other visual system disturbances as well. They invariably complain of poor vision yet test at 20/20 in the ophthalmologist's office. Recently I saw a patient who had received three different eyeglass prescriptions in less than one year because of a failure to diagnose PSP. The visual problem is due to midbrain processing dysfunction and is not a correctable lens problem. Patients never complain that they can't move their eyes properly. Dementia is com-

mon in PSP but not universal. Treatment provides very limited benefit.

Less Common Akinetic Rigid Syndromes

Other akinetic rigid syndromes mistaken for PD include normal pressure hydrocephalus (NPH)⁴ and Binswanger's disease.^{5,6} NPH represents a triad of dementia, urinary incontinence and gait dysfunction in which patients suffer from a "magnetic gait," walking as if their feet were stuck to the ground. Although the gait is often described as "ataxic," it is not. Binswanger's disease is a poorly characterized entity which is a multi-infarct state in which parkinsonism occurs "from the waist down" (ie, the legs and gait are parkinsonian and often somewhat ataxic while the upper body has none of the typical features of this disease). Striato-nigral degeneration is a disorder that mimics PD except for its lack of response to the PD medications.⁷ The pathologic lesions are seen in the substantia nigra, as in PD, but also in the striatum (caudate nucleus and putamen), which is not structurally affected in PD. Since this is the location where dopamine works in PD, L-DOPA and dopamine agonists have no effect in striato-nigral degeneration since there are no remaining neurons sensitive to dopamine action.

Cortico-basal Ganglionic Degeneration — A "New" Disorder

Those of us who see large number of PD patients often wonder how frequently our "atypical" PD cases represent an undescribed syndrome that currently eludes us, but will be clear to future clinicians. It is reported that the late Houston Merritt, a great neurological clinician, queried, after reading the initial report describ-

ing PSP, that if PSP is so common in Canada, why wasn't it seen in New York? Of course, it was, but it hadn't been recognized. A newly identified syndrome that has only recently gained attention is cortico-basal ganglionic degeneration.⁸ It is not yet known whether this syndrome has a uniform pathologic substrate or represents, as with parkinsonism, a variety of different diseases with similar phenomenologies. As its name suggests, patients develop signs of degeneration in cortical as well as basal ganglionic function. Since recognizing my first case three years ago I have seen seven patients with this disease. The typical abnormalities include progressive aphasia and/or apraxia, parkinsonian gait, dystonia and rigidity.^{8,9} In a manner quite unusual for a cerebral degeneration, there is a striking asymmetry to the progression, falsely leading the neurologist, seeing the patient for the first time, to believe one or more strokes had occurred, dismissing the patient's history of slow progression. There may be one arm and a contralateral leg involved far out of proportion to the paired limbs. The patients develop a peculiar rigidity which increases with passive movement and is often associated with passive, movement-induced myoclonus, simulating a tremor.

Tremors

The most common cause for an incorrect diagnosis of PD is essential (or familial) tremor. This disorder, so perfectly exemplified by Katharine Hepburn in her performance in "On Golden Pond," is usually inherited as an autosomal dominant trait. (Katharine Hepburn actually has the disorder.) Classically it involves the hands, worsens with anxiety and is relieved by alcohol. One frequently hears of patients who,

having discovered the beneficial effects of ethanol, require increasing doses of this drug, or of the patient who takes a drink before rather than during the cocktail party. The tremor is present with movements and on holding sustained postures but is rarely present when the arms are at rest, in contrast to PD in which the tremors are present at rest and resolve with movement. Essential tremor often involves the head, causing a "yes" or "no" head movement, distinguishing it from PD which almost always spares the head. Finally, essential tremor frequently involves the voice, causing a vocal quivering, but without dysarthria, loss of volume, stuttering or hesitancy, as is commonly present in PD.

Essential tremor responds best to ethanol but, to some extent, also to propranolol, primidone and phenobarbital.¹⁰ Response is often disappointing since it is rare for the tremor to resolve completely. The amplitude of the movements does lessen, however.

Huntington's Disease

Huntington's Disease (HD) represents one of the most feared of human disorders.¹¹ It is an autosomally dominant inherited trait with complete penetrance so that a carrier will be affected if he/she survives long enough.

In sufficiently large kindreds laboratory tests may now identify clinically normal carriers. This provides a means by which members of HD family may determine, with a great degree of confidence, whether or not they are free of the HD gene. This is of crucial importance in deciding whether or not to have offspring but for those unfortunate enough to be gene positive the new knowledge can be devastating.¹² HD has a highly variable age of onset and the age of onset in the parent does not predict the onset in the child.

Generally the first signs occur after the procreative years so that a parent first takes ill after several children are born. A carrier may develop the disease shortly after discovering his status, or may die of other causes late in life, untouched by HD. Most however develop the disorder in middle age.

The diagnosis of Huntington's disease rests on clinical findings and the family history. The only supportive laboratory finding, late in the course, is caudate nucleus atrophy as seen on a CT scan of the brain.

HD causes a triad of chorea, dementia and behavioral disturbances including psychosis. The premorbid personality is normal and one recalls the tremendous creativity of Woody Guthrie as an illustration of how gifted a person may be before the ravages of disease begin. Treatment of the illness is limited to genetic counselling and behavioral control. Although physicians are inclined to treat the chorea with dopamine blocking agents, it appears that motoric disability is related not to the chorea but to a progressive dystonia which is likely to worsen with these drugs. It is interesting to note that HD patients, in addition to chorea, also develop the rigidity generally seen in PD as well as the dystonia. When HD begins in childhood in fact, it typically begins as a parkinsonian rather than a choreic syndrome, for unknown reasons.

The diagnosis of HD rests on clinical findings and the family history. The only supportive laboratory finding late in the course is caudate nucleus atrophy as seen on a CT scan of the brain. Although HD is not a rare disorder and has been identified in vir-

tually all ethnic groups, there have been no verified new mutations. Every pathologically verified case has had either known parental involvement or the parental status has been unknown. Thus the frequency of spontaneous mutations must be extremely small.

In isolated cases of phenotypic HD but without family history one assumes that either the diagnosis is inaccurate or that the family history is incomplete (ie, parents may have died or disappeared before disease onset or the biologic parents may be unknown).

Unusual Phenomenologies

Dystonias

Dystonia describes a sustained abnormal posture, or slow turning movement caused by prolonged contraction of antagonist muscles. It is frequently associated with tremors or sudden, jerking movements of the involved body part. It can be generalized, involving the whole body as is the case in the hereditary form of this illness, but it may also involve isolated parts of the body. The most commonly recognized form of dystonia is torticollis or "wry neck," in which the subject's neck is involuntarily turned, either spasmodically or constantly. Usually the turning is to one side but it may be in extension, flexion, or lateral flexion and with variable degrees of rotation.

Other dystonias, often incorrectly identified as being psychiatric in origin, involve isolated body parts and may occur only with very specific movements. Writer's cramp is a dystonia brought on by attempting to write. The fingers may flex or extend and the more proximal muscles tighten, rendering the act of writing difficult or impossible. Yet the same person might be able to type, use fine instruments or thread a needle with the same

hand. I saw a young man recently who had a markedly abnormal gait because of generalized dystonia but could roller skate without difficulty. Often these patients have "sensory tricks." Touching certain places, or performing a substitute action will abort the dystonia. For example, a torticollis patient will touch his chin lightly to prevent the head from turning, or a patient will reach for an object using an intricate maneuver rather than a direct route.

Blepharospasm, the involuntary closing of the eyelids, is one dystonic disorder that responds to therapy. Patients with this syndrome are frequently blinded by their inability to open their eyelids unless they pry them open with their fingers. Recent experience revealed a dramatic response to local injections into the lids of botulinum toxin.¹³ This bizarre approach weakens the muscles sufficiently to allow the lids to remain open, yet when used appropriately doesn't cause disabling ptosis. The therapeutic response persists for 2-4 months and so far no one thus treated has developed weakness elsewhere in the body. Attempts to use botulinum toxin (Botox) in torticollis and other dystonias have produced only mild success.

Tics

Tics are rapid jerks, involving discrete muscle groups, generally lasting less than 0.1 second. They are extremely common in children, displayed as excessive blinking, nose wrinkling, eye opening, sniffing or shoulder shrugging and have a benign prognosis. When vocalizations accompany the body movements the syndrome is called Gilles de la Tourette's syndrome (GTS). This is frequently inherited, but not always, and is often associated with behavioral abnormalities. In such children attentional

deficit disorders are common and in both adults and children obessional behaviors are often encountered.

Although the popular conception of Gilles de la Tourette's syndrome brings to mind a barking, cursing child who has pronounced emotional problems, this is rarely the case.

Tics in GTS can be very complex but are nonetheless stereotyped. Patients may throw themselves on the floor or move in bizarre ways, invariably as a rapid sequence of gestures. They can be voluntarily controlled to a limited extent, with the analogy often being made of cough suppression in a silent concert hall. The tic can be suppressed for a time but then a volley of movements will inevitably occur. The vocalizations are generally coughs, sniffs, and grunts but barking and cursing occur in a minority of subjects, giving the syndrome its notoriety. Occasionally, involuntary mimicking of gestures or sounds occur as well. As in most movement disorders the tics and utterances worsen with stress but unlike other disorders, many tics worsen when the patient is isolated and relaxed with no one present to observe them. At such times the subject can allow free rein to the tics letting them surface without restraint, thus providing a sense of relief to the sufferer who no longer has to struggle to restrain them.

Tics in children rarely merit treatment; however, occasional cases of GTS may require therapy when the tics become debilitating. In such cases the initial drug of choice is clonidine, with neuroleptics such as pimozide and haloperidol used as secondary

agents. Although the popular conception of GTS brings to mind a barking, cursing child who has pronounced emotional problems, this is rarely the case. Famous people who have been successful despite this affliction include Samuel Johnson and at least two current outstanding professional athletes.

Paroxysmal Disorders

The paroxysmal movements are not seizure disorders and most likely result from an abnormal biochemical accumulation rather than as the result of an abnormal electrical discharge. Many of these childhood disorders occur as parts of inborn errors of metabolism and are not likely to be missed in this context. However, some of the syndromes occur in isolation and there are few clues to explain their pathophysiology.

Paroxysmal familial ataxia is a non-progressive disorder that appears to be inherited as an autosomal dominant gene. The affected individual has episodes, usually lasting one to several hours, of pure cerebellar dysfunction. Subjects develop nystagmus and gait ataxia without impairment of thinking and without weakness. These are usually misdiagnosed as seizures, basilar migraines (although no headache occurs) or as functional disorders. Most patients experience complete resolution of symptoms when treated with acetazolamide, a serendipitous discovery made when a patient was misdiagnosed as having a different illness.¹⁴

Psychogenic movement disorders, often disabling, are being increasingly recognized.

Paroxysmal dystonia¹⁶ and choreoathetosis¹⁷ are yet other

syndromes that occur, either on a sporadic or familial basis. These disorders have a highly variable duration, lasting from a second (personally observed case) to several hours. Unlike the paroxysmal ataxic syndrome these are less responsive to medication.

Non-Organic Movement Disorders

Neurologists increasingly recognize the non-physiologic basis for some instances of disorders of movement. Not long ago, many currently recognized neurologic problems, especially the dystonias, were believed to be psychogenic. These included torticollis and writer's cramp. It is very easy to understand why these were so categorized, since the distorted appearance is often so bizarre and the person, often afflicted for several years, is told repeatedly that the disorder is psychosomatic. Psychogenic movement disorders, often disabling, are being increasingly recognized,^{18, 19} including psychogenic PD, tremors, torsion dystonia, facial dystonia and hemifacial spasm.²⁰ The problems with diagnosis may be profound and different observers may come to different conclusions. Laboratory studies are not helpful and diagnosis rests on clinical acumen alone.

References

- ¹ Ward CD: Brain 1988;111:1247.
- ² Jellinger K: The pathology of Parkinsonism. In Marsden CD, Fahn S (eds) Movement Disorder 2, Butterworths, Ltd., Boston, 1987.
- ³ Steele JC, Richardson JC, Olszewski J: Progressive supranuclear palsy: A heterogeneous degeneration involving the brainstem, basal ganglia and cerebellum, with vertical gaze and pseudobulbar palsy, nuchal dystonia and dementia. Arch Neurol 1964;10:333-359.
- ⁴ Fisher CM: Hydrocephalus as a cause of gait disorders in the elderly. Neurology 1982;32:1358-1363.
- ⁵ Caplan LR, Schoene WC: Clinical features of subcortical arteriosclerotic encephalopathy (Binswanger's Disease). Neurology 1978;28:1206-1215.
- ⁶ Thompson PD, Marsden CD: Gait Disorder

of Subcortical Arteriosclerotic Encephalopathy: Binswanger's Disease. Movement Disorders 1987;2:1-8.

- ⁷ Adams RD, Salam-Adams M: Striatonigral degeneration. In Vinken PJ, Bruyn GW, Klawans HL (eds): Handbook of Clinical Neurology Vol. 49. Elsevier Science Publishers, New York, 1986.
- ⁸ Rebeiz JJ, Kolodny EH, Richardson EP: Corticodentatonigral Degeneration With Neuronal Achromasia. Arch Neurology 1968;18:20-23.
- ⁹ LeWitt P, Friedman J, Nutt J, Corczyn A, et al: Progressive rigidity with apraxia: The variety of clinical and pathological features. Neurology 1989;39 (Suppl 1):140.
- ¹⁰ Findley LJ: The pharmacology of essential tremor. In Marsden CD, Fahn S (eds). Movement Disorders 2. Butterworths and Co., Ltd., Boston, 1987.
- ¹¹ Penney JB, Young AB: Huntington's Disease. In Parkinson's Disease and Movement Disorders. Jankovic J, Tolosa E (eds). Urban and Schwarzenberg, Baltimore, MD 1988.
- ¹² Brandt J, Quaid KA, Folstein SE, et al: Presymptomatic diagnosis of delayed-onset disease with linked DNA markers. The experience in Huntington's Disease. JAMA 1989;261:3108-3114.
- ¹³ Elston JS: Botulinum Toxin Treatment of Blepharospasm. Adv Neurol 1988;50:579-582.

¹⁴ Griggs RC, Moxley RT, Lafrance RA, McQuillen J: Hereditary Paroxysmal Ataxia: Response to Acetazolamide. Neurology 1978;28:1259-1264.

¹⁵ Friedman JH, Hollmann PA: Acetazolamide Responsive Hereditary Paroxysmal Ataxia. Movement Disorders 1987;2:67-72.

¹⁶ Lance JW: Familial Paroxysmal Dystonic Choreoathetosis and Its Differentiation from Related Syndromes. Ann Neurol 1977;2:285-293.

¹⁷ Mount LA, Reback S: Familial Paroxysmal Choreoathetosis: Preliminary Report on a Hitherto Undescribed Clinical Syndrome. Arch Neurol and Psych 1940;44:841-847.

¹⁸ Koller W, Lang A, Vetere-Overfield B, et al: Psychogenic tremors. Neurology 1986;39:1094-1099.

¹⁹ Fahn S, Williams PJ: Psychogenic dystonia. Adv Neurol 1988;50:431-455.

²⁰ Friedman, JH: Personal observations.

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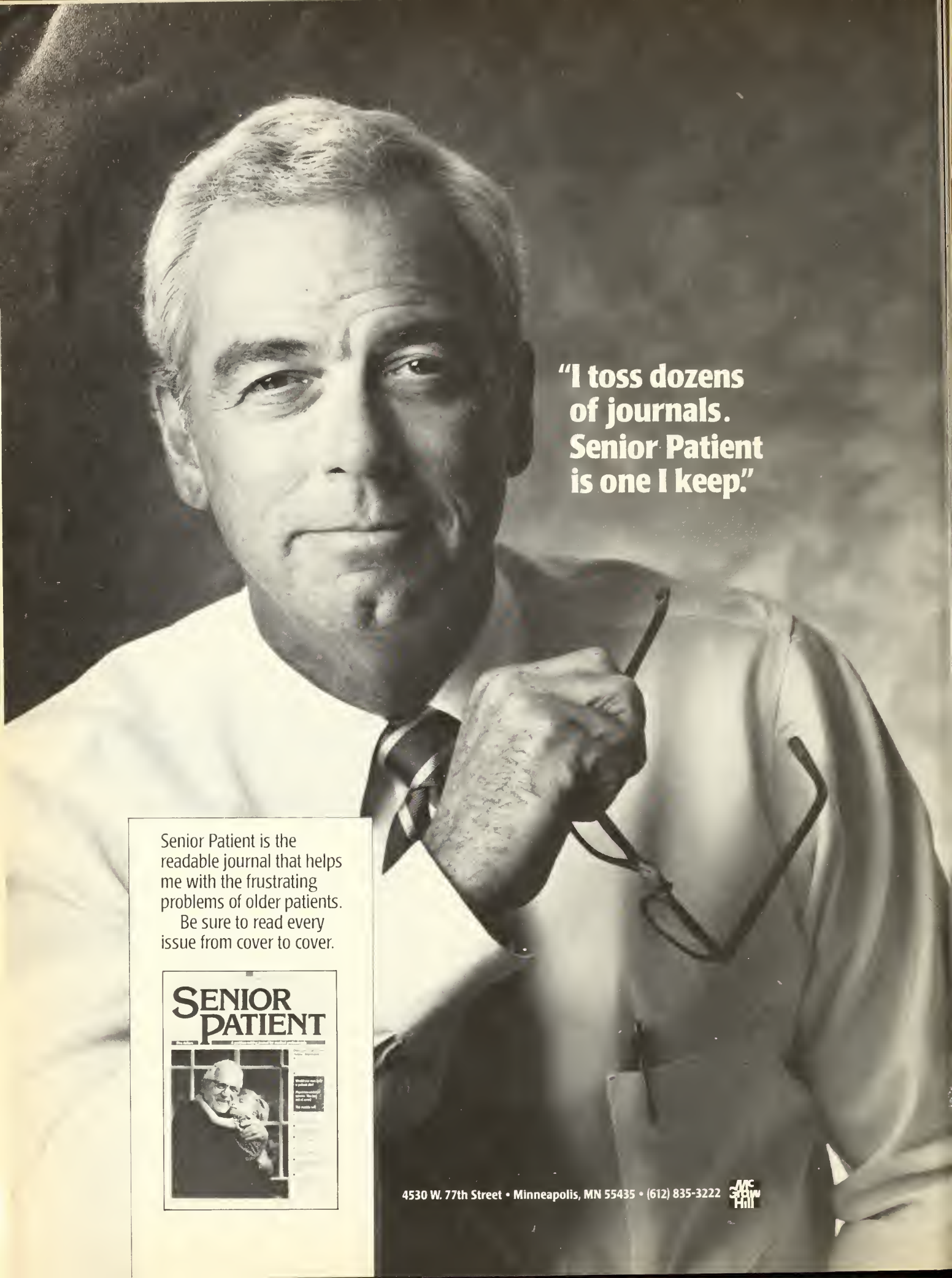
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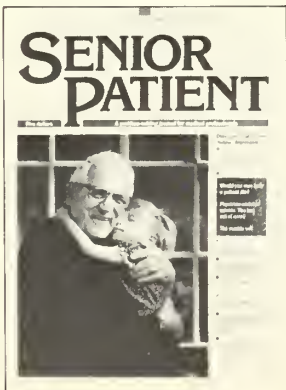
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Under Your Calvarium

Brown University Program in Medicine 1989 Commencement Speech

Tom J. Wachtel, MD

You will now, more than ever before, have to rely on your minds to do the best job you can.

I am greatly honored to have been asked to deliver your last lecture in medical school. I have been invited to present papers at many meetings of professional organizations, but no invitation to speak has ever given me more pleasure than this one. I view myself more as a teacher than an investigator; and being your commencement speaker is the highest reward for my efforts. Thank you very much.

The Dean's Office insisted that I provide a title for my talk before I had any idea of what I was going to say, and so the title is "Under Your Calvarium." For the lay people in this audience, the calvarium is the top of the skull. It covers and protects the brain. After seven or eight years under the Elms of this campus and others, we are turning you loose with your hard-earned MD degree. Having lost the protection of the Elms, you will now, more than ever before, have to rely on your minds to do the best job you can.

Just six months ago I was called to see a fifteen-year-old high school student with a rash. I diagnosed a staphylococcal skin infection, bullous impetigo, and

quickly proceeded to write a mindless prescription for the antibiotic dicloxacillin. A month later, the impetigo recurred, and I treated her similarly over the phone after her mother assured me that the rash was the same. Again, the rash resolved promptly. Four weeks later, I received another call from her mother. The rash was back. This time I became concerned and decided to put my mind to work. I remembered that the three basic elements to consider in infectious diseases are the host (who is the patient), the bug (which is a bacteria or a virus), and the drug. I had no concerns about using dicloxacillin for staphylococcus — it's the right drug and it had worked twice before for this bug. The host was of more concern to me. Could something be wrong with her immune system? Is she sexually active? Might she be using illicit drugs? Could she have AIDS? Rather than prescribing dicloxacillin mindlessly for a third time, I decided to see the patient; and since I didn't have office hours that day, I made a house call. The house was immaculate; knick-knacks were neatly aligned on the shelves, and the floors sparkled. Then I stepped into the patient's room; what a contrast! Books, stuffed animals, clothes were scattered all over the place, covered with dust; in brief,

a war zone. We had an open discussion: she was not sexually active, and did not use drugs. I believed her. As we talked, I noticed a jar of Eucerin cream and a tube of cortisone, both of which she used periodically for eczema. I opened the Eucerin jar and there was the answer for the staphylococcal impetigo. The jar was 18-months-old and the cream was filthy. I supervised the disposal of the topicals and wrote my third prescription for dicloxacillin. The impetigo has not recurred thus far. The moral of this story is that the facts alone regarding staphylococcal skin infections which I was taught in medical school or during my later readings would not have enabled me to cure this patient. Mindfulness did.

Mindfulness is the latest fad in psychology. Pioneered by Ellen Langer,¹ a Harvard psychology professor, followers have already raised Mindfulness to the heights of Freud's psychoanalytical techniques or Skinner's behaviorism.

Dr Langer narrates the following three-generation story of mindlessness:

"One day a woman was about to cook a roast. Before putting it in the pot, she cut off a small slice. When asked why she did this, she said it was because her mother had always done the same thing when she cooked a roast. Her own curiosity aroused, she tele-

Tom J. Wachtel, MD, is Associate Professor, Community Health, Brown University Program in Medicine, Providence, Rhode Island.

phoned her mother to ask why she always cut off a little slice before cooking her roast. The mother's answer was the same, 'because that's the way my mother did it.' Finally, in need of a more helpful answer, she asked her grandmother why she always cut off a little slice before cooking a roast. Without hesitating, her grandmother replied, 'because that's the only way it would fit in my pot.' "

Mindlessness . . . is simply the inevitable, yet correctable, result of institutionalizing inflexible systems, rules and behaviors.

Let me tell you another story:

When a new library was built at the University of California at Berkeley, the architect evidently designed the building with an insufficient number of elevators. Soon after the construction was completed, complaints began to pour into the librarian's office because people, during peak hours, had to wait several minutes to get onto an elevator. So the University hired a construction engineering firm which drew up plans for additional elevators at a cost of several million dollars. Just as the contract was being put up for bids, a mindful junior member of the consulting firm suggested that mirrors be placed near the elevators on each floor. This was done and the flow of complaints promptly stopped. This is a great example of how the power of context can inhibit creativity. The University and the engineering firm narrowly defined the problem as one of insufficient elevator capacity when, in reality, the problem was people's boredom, waiting for the elevator, and this could be corrected easily by appealing to their vanity.

Along the same lines, some of

you may recall Theodore Levitt's classic paper entitled "Marketing Myopia"² where he attributes the decline of American railroads to their self-perceived narrow function of being in the railroad business rather than the transportation business.

Getting back to our careers in medicine, I have often felt guilty for not having read a journal article that is being discussed by colleagues in the hospital cafeteria. You will not be able to keep up with the medical literature either. This will be true whether you have chosen to become generalists or specialists, and you might feel guilty, too. The explosion of medical information is more likely to accelerate than to stabilize. Fortunately, as fast as it grows, computer technology is making it easier for us to access it. I am not suggesting here that you should not continue to learn new facts and new technologies, but I am warning you that keeping up with the tide of new developments in medicine is a battle that you will continue to fight and continue to lose.

For me, being mindful about my life outside of medicine has helped me deal with misplaced guilt about failing to keep up with the literature. (Let's call it mindless guilt.) My guilt originated in seeing myself as having had a choice of either reading or not reading the important article that my colleagues were discussing, and having stupidly made the wrong choice.¹ I, like Ellen Langer, now believe that I felt guilty because I was fixated on the outcome of my choice. Had I not been so fixated, I would have realized that the choice was not between reading the article and doing nothing, but rather between reading the article or cooking dinner, or taking a much-needed rest, or reading to my daughter. My guilt was rooted in

a faulty comparison.

Ellen Langer blames our educational system for this type of mindlessness.¹ Indeed the focus of schooling is usually on acquiring knowledge rather than the process whereby knowledge is acquired. This single-minded pursuit of one outcome or another begins in kindergarten, where I, and now my daughter, were taught to sing the alphabet and were left wondering what an LMNOP is. It continues through medical school where we spend nights and days memorizing facts, facts, and more facts . . . at least what were accepted as facts, when they were given. This method of education does not foster a mindful attitude about our professional or private lives. Mindlessness is not to be confused with stupidity or laziness; it is simply the inevitable, yet correctable, result of institutionalizing inflexible systems, rules and behaviors. For doctors, the roots of mindlessness include repetition, premature cognitive commitments and education where facts are presented unconditionally.

Keeping up with the tide of new developments in medicine is a battle that you will continue to fight and continue to lose.

Marcus Aurelius, a Roman Emperor and philosopher said "Our life is what our thoughts make it." Awareness of the process of making real choices along the way of our careers and our lives enables us to feel better about our choices. After all, mindful choices are perceived to offer some benefits, or else why would we intentionally make them?

Opportunities to practice mindlessly or mindfully abound in every day medical practice.

Let's consider a patient with mild hypertension. The practice guideline of the Joint National Committee on detection, evaluation and treatment of hypertension, a consensus panel of experts, encourages mindless practice: Forget the patient, get that diastolic pressure below 90. The pharmaceutical representative is sitting in your waiting room prepared to sell you the newest, most effective, best-tolerated, me-too anti-hypertensive drug. He'll give you a pen, a clock and a calculator, all with the drug's name on them, and if you prescribe enough of this new medication, you might be offered a trip to a medical conference in Martinique during which you will have additional opportunities to hear about the merits of this and other new drugs.

You are being set up for a career of mindless practice. But you do not have to fall into that trap. Simply remember that your mildly hypertensive patient is a person with a risk factor for stroke and heart disease: he or she is not a diastolic pressure to knock down with a new pill. Now you have the ingredients to practice mindfully. A 1988 paper published by Brown Faculty³ reminds us of some basic issues to consider before earning a few bonus points toward your drug company-sponsored trip to the Caribbean.

Why not to treat mild hypertension:

First: Treatment controversies continue despite massive research.

Second: Altering favorably a disease process or a risk factor does not imply that overall health or risk is altered favorably.

Third: The vast majority of mildly hypertensive patients will not have a resulting improvement in measured morbidity or mortality. This is the issue that we

discussed in class contrasting relative risk and absolute risk. A relative 20 percent reduction in mortality translates into "if 850 mildly hypertensive patients are given anti-hypertensive drugs for one year, one stroke will be prevented." Emphasis on population-wide benefits can distort decision-making that is intended to benefit an individual patient.

Fourth: Diagnosis and treatment have effects on much more than the cardiovascular end points that are usually measured and reported in the medical literature. Altered self-perception, illness behavior, economic costs, drug side-effects and other problems may have a substantial impact on a person's life and well-being.

I am not suggesting that the mindful doctor should not treat mild hypertension. The reasons to treat are well-established. What I am suggesting is that the doctor consider all the factors that are critical in the determination of whether treatment will serve a patient's best overall interest. For one patient, taking daily medication may be a burden that reinforces fear or illness behaviors; for another, it may confer a sense of increased protection or of pride in one's own health habits. To prescribe medication systematically for all patients with mild hypertension is mindless. The potential gain of a few days of additional life at some distant time in the future must be weighed by the mindful doctor against side effects which are immediate and often times disabling, such as fatigue, dizziness, or impotence, to name a few, and against the cost of the medication.

This brings me to my final point. Over the next decade, you are going to witness the development of practice guidelines, protocols,

algorithms. As you may know, this is my own area of investigation. My fear is that regulations, third parties, medical review boards will threaten our autonomy by linking adherence to guidelines with such factors as reimbursement and licensure. . . . On the other hand, guidelines have the potential to streamline those areas of care which are the least controversial and give us more time to consider mindful medical decisions that require judgment.

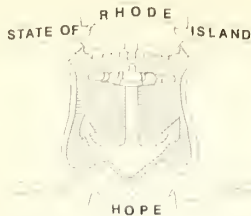
We all agree that automatic pilots in airplanes have made air travel safer but no one here would travel in an aircraft without a pilot. I see practice guidelines as the equivalent in medicine of the automatic pilot. They can allow us to focus our minds where mindfulness is most needed.

I see practice guidelines as the equivalent in medicine of the automatic pilot. They can allow us to focus our minds where mindfulness is most needed.

As you may recall from the Community Health Clerkship, I do not recommend any reading prior to my lectures. The reason is that I firmly believe that the process of learning the information, using practical examples and student-teacher interactions in the classroom, is more important than the information itself as presented in a textbook. I want students to be mindful in my class. I wish you, as doctors, to be mindful at the bedside and in your office. This will allow you to grow, be satisfied and succeed in your careers.

References

- ¹ Langer EJ: Mindfulness. Addison-Wesley Publishing Co Inc 1989.
- ² Levitt T: Marketing Myopia. Harvard Business Review 1960; 38:45-56.
- ³ Forrow L, Wartman S, Brock D: Science, Ethics and the Making of Clinical Decisions. JAMA 1988; 259, 21:3161-3167.



HEALTH BY NUMBERS

Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

Level of Functional Impairment among Nursing Home Residents in Rhode Island

Severe impairments in normal daily activities often exhaust the abilities of an individual to live independently, strain the capabilities of caregivers, and lead to nursing home placement. In Rhode Island, about seven percent of those 65 years or older reside in nursing homes in-state.

About 71 percent of nursing home residents in a census taken 31 December 1987 were beneficiaries of the Rhode Island Medical Assistance Program (Medicaid).¹ As part of the Medicaid certification procedure for nursing homes, an annual review of all Medicaid-covered nursing home residents is conducted in Rhode Island on an ongoing basis by the Division of Facilities Regulation of the Rhode Island Department of Health. In the survey conducted between July 1987 and June 1988, data were collected from 6,505 Medicaid-funded nursing home residents.

The activities of daily living (ADL) index used here is based on ability to perform six normal functions or without assistance — eating, continence, transferring from bed to chair, going to the toilet, dressing, and bathing.² Figure 1 shows the frequency of each of the specific activities used in the index for three levels of functional impairment (mild [0-2 ADLs], moderate [3-4 ADLs], and severe [5-6 ADLs]). In general, the highest proportion lose the ability to bathe independently or without assistance first

(81 percent of those impaired in no more than two ADLs are unable to do so). Next, the ability to dress oneself is lost (42 percent of those with no more than two ADLs and 92 percent of those with three or four ADLs are unable to do so). Then individuals become unable to use the toilet and/or to move from the bed to a chair (transferring) independently. About three-quarters of those with three to four ADLs cannot perform either activity without assistance. Next, the ability to control discharge of urine or feces on a regular basis is lost (less than 50 percent are regularly incontinent among those with four or fewer ADLs, rising to 91 percent for those with five or six ADLs). Finally, the ability to feed oneself is lost (92 percent of those with fewer than six ADLs are able to feed themselves).

As seen in Figure 2, at the time of the survey, over one-third of Medicaid-enrolled nursing home residents were mildly impaired. Those who were unimpaired (0 ADLs) include individuals with mental problems: 26 percent of the unimpaired display "inappropriate" behavior, and another five percent are hearing or sight impaired. About 18 percent of the sample were moderately impaired, and 44 percent were severely impaired. The low percentage of residents who were moderately impaired may reflect quicker movement between levels of impairment for individuals in this middle category.

Figure 3 shows changes in functional status between the date of admission and the survey date. The median time between the most recent admission and the survey — the current length of stay — was 18 months. Nearly two-thirds (65 percent) of residents were found to have had the same ADL status at admission and at review. Another 13 percent had improved in status during this time, and nearly one-quarter (22 percent) had become more impaired. Overall, ADL status at the time of the survey is strongly related to ADL status at admission ($r = 0.826$). Thus, nursing home admission does not necessarily signal a rapid progression towards death for most patients.

References

- Unpublished data from the Short and Long Range Planning survey of licensed nursing facilities for the period 1 January to 31 December 1987, Division of Health Systems Development, Rhode Island Department of Health.
- Katz, S. and Akpom, C.A. Measures of primary sociobiological functions, *International Journal of Health Services* 1976;6(3), 394-506.

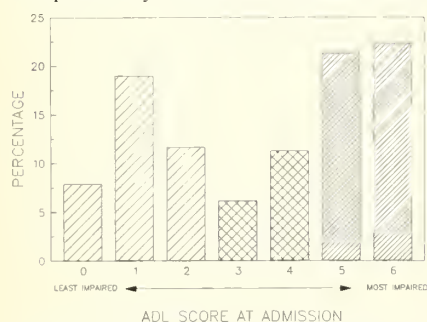


Figure 1. Percentage Unable to Perform Activities of Daily Living by Level of Functional Impairment, Medicaid-enrolled Nursing Home Residents, Rhode Island, 1987-1988

ACTIVITY OF DAILY LIVING	LEVEL OF FUNCTIONAL IMPAIRMENT		
	NONE OR MILD (0-2 ADLs)	MODERATE (3-4 ADLs)	SEVERE (5-6 ADLs)
BATHING	80.6%	99.2%	99.6%
DRESSING	42.2%	92.0%	99.4%
TOILET	12.8%	74.5%	97.0%
TRANSFER	12.5%	70.5%	97.1%
CONTINENCE	9.4%	46.2%	90.8%
EATING	3.9%	7.7%	49.4%

Figure 2. Distribution of Medicaid-enrolled Nursing Home Residents by the Index of Activities of Daily Living, Rhode Island, 1987-1988

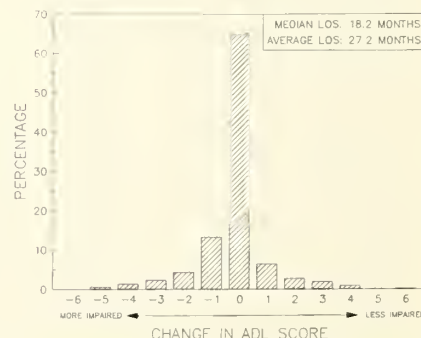
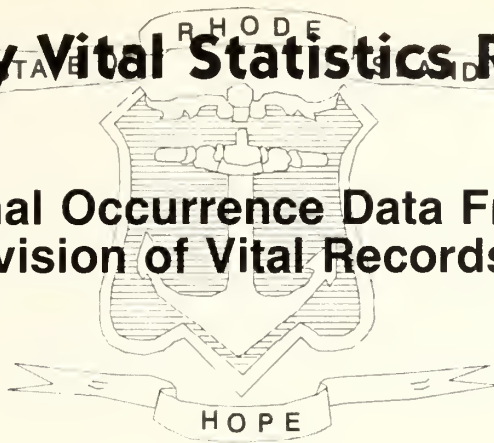


Figure 3. Change in Activities of Daily Living Status at Admission and at Review, 1987-1988, among Medicaid-enrolled Nursing Home Residents, Rhode Island

Submitted by the Office of Health Statistics, Jay S. Buechner, Ph.D., Chief. Patient Care and Services Survey data were provided by the Division of Facilities Regulation, Wayne Farrington, Chief.

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records



H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with October 1989	
	October 1989 Number	Number	Rates
Live Births	1,371	15,082	15.2*
Deaths	876	9,761	9.8*
Infant deaths	(19)	(153)	10.1†
Neonatal deaths	(16)	(119)	7.9†
Marriages	983	8,208	8.3*
Divorces	320	3,656	3.7*
Induced Terminations	626	7,921	525.2†
Spontaneous Fetal Deaths	92	1,121	74.3†
Under 20 weeks' gestation	(82)	(1,002)	66.4†
20+ weeks' gestation	(10)	(107)	7.1†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with July 1989		
	July 1989 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	245	3,456	348.0	4,575.5
Malignant Neoplasms	195	2,422	243.9	7,650.5
Cerebrovascular Diseases	44	609	61.3	1,157.0
Injuries (Accident, Suicide, Homicide)	37	427	43.0	9,957.5
COPD	20	296	29.8	366.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

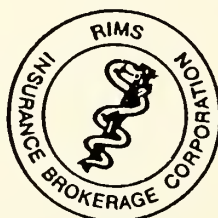
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THE RHODE ISLAND MEDICAL JOURNAL

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Issued Monthly under the direction of the Publication Committee

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (February, 1940)

The lead article represents an address given by Charles Fitzpatrick MD, Superintendent of the Rhode Island State Hospital for Mental Diseases at Howard, which provides the readership with a brief history of the mental hygiene movement, both internationally and locally, and outlines the need for enhanced state funding so as to avoid the hazards of overcrowding of the inpatient psychiatric facilities administered by Rhode Island. The article begins with a description of the pioneering labors of Pinel in unshackling the psychiatric patients at Bicetre and the humane efforts of the English Society of Friends and Dr William Tuke in establishing the York Retreat.

"The beginning of the nineteenth century saw only four institutions devoted to the care of the mentally ill in the whole country (United States), and of these only one had been built by a government authority. These early institutions were located in Philadelphia (1752), Williamsburg, Virginia (1773), New York (1791), and Baltimore (1797). In 1817, the Society of Friends in Philadelphia opened a second hospital in that city modeled on the lines of the York Retreat. In New England a year later the McLean Hospital was opened at Somerville, Massachusetts. In 1824, the Hartford Retreat and in 1830 the asylum at Worcester, which is now the

Worcester State Hospital was opened for the reception of patients. All these institutions were actuated in their treatment by the new scientific and humane ideas inaugurated by Pinel and Tuke."

"The first mention of insanity in the enactments of the Rhode Island General Assembly was in 1725, when a statute was enacted whereby the towns on the mainland of Rhode Island were empowered to build a house of correction for vagrants and to keep mad persons in. In 1742, the care of the insane and imbeciles was given over to the town councils. The opening of the Dexter Asylum in 1828 offered slight alleviation in the conditions surrounding the care of the mentally ill of the City of Providence."

In 1841, in a codicil to his will, Nicholas Brown set aside the sum of \$30,000, "... toward the erection or endowment of an insane or lunatic hospital or retreat." A few months later Cyrus Butler, a prosperous local merchant, gave \$40,000 for this same purpose, and in November of 1844 the corporation for the Butler Hospital for the Insane was established in Providence. Dorothea Dix, the eminent nineteenth century humanitarian, was probably instrumental in persuading Butler to direct his philanthropy to the help of the mentally ill population. The first superintendent of the hospital was the distinguished physician, Dr Isaac Ray, an authority on medical jurisprudence and the author of, 'Mental Hygiene.'

Fitzpatrick enumerates the following institutional facilities for the care of emotional disorders in Rhode Island at the time of his speech (January 9, 1940): The Emma Pendelton Bradley Hospital; the Chapin Hospital, psychiatric service; the Butler Hospital; the Out-Patient Department of the Rhode Island Hospital; and the State Hospital in Howard, "... which at the present time has approximately 2,800 patients. The staff presently concerned in the care and management of these patients now numbers 535 persons."

An editorial recommends that practicing physicians have an obligation to become supporting members of the Rhode Island Medical Society. The annual dues (ten dollars) provides support for an extensive medical library housed in the Society's headquarters.

The following slate of officers is proposed for 1940: For President, John G. Walsh, MD; for Vice-President, Murray S. Danforth, MD; for Secretary, Harman A. Lawson, MD; for Treasurer, William P. Davis, MD and for the Executive Committee, Harry C. Messenger, MD and Andrew W. Mahoney, MD.

Twenty-Five Years Ago (February, 1965)

The lead article is the Presidential address before the Providence Medical Association, by Frank I. Matteo, MD, and entitled, "The Role of Our Association in a Changing World: Retrospect and

Prospect." The address outlines the many public health successes recently achieved in Rhode Island, particularly those involving mass immunization and the dramatic reduction in maternal mortality rates.

The seventh Murray S. Danforth Oration is presented by Edwin F. Cave, MD, on the subject of "Healing of Fractures and Nonunion of Bone." It is a detailed description of the pathophysiology of fracture healing, the causes of delayed bone union and nonunion, the role of bone grafting, the management of cases of nonunion, and illustrative examples of nonunion with radiographic amplification.

E. Franklin Hall, MD, provides an article on the medical aspects of driver safety and driver licensing, proposing a medical advisory committee to consult with the motor vehicle authorities regarding the medical fitness of drivers. The recommendations are distilled from the deliberations of a three-day meeting of the American Medical Association, the American Association of Motor Vehicle Administrators and the United States Public Health Service. This meeting was prompted by "... more than 40,000 motor vehicle fatalities annually and three million injuries, disfigurements, and permanent impairments each year. ..." The basic purpose of the meeting is to: "Develop better understanding of the complex relationships between driving ability and drugs and medicines, vision problems, lapses of consciousness and effects of specific diseases."

An editorial talks of "... the entrance of a new physical or chemical modality" to join the other remarkable advances of the decade of the 1960s which has seen the development of "... extracorporeal circulation, ultrasonics, cryophysics, nucleopro-

tein chemistry, hyperbaric oxygenation and other diverse entities." The new modality, Light Amplification by Stimulated Emission of Radiation, is more simply called, *laser*. The editorial summarizes the development and possible uses of this new capability. Yet another editorial talks of a new and exciting development in postgraduate education for the practicing physician called, "Programmed Instruction." The editorial concludes, "A first-rate program with its high degree of logic, organization, and coherence provides a welcome addition to the methods of keeping up."

An historical note observes that telephone numbers were born in 1880 when Dr Moses Greeley Parker, a practitioner in Lowell, Massachusetts, proposed the use of numbers in place of the 200 subscriber names. He recommended

this during a raging measles epidemic observing that telephone communications would cease should the town's four telephone operators succumb.

The American Hospital Association states that hospital costs rose 11% in the past year, "... averaging \$38.91 per patient per day. This hospitalization cost varied considerably among states, ranging from a low of \$26.07 in South Carolina to a high of \$51.95 in California. (The average cost per patient day in Rhode Island is \$44.11.) When these figures are multiplied by the average length of patient stay, New York's high of 9.7 days gave it the top figure of \$426.61 for the average cost per patient stay. (The average cost per hospital stay in Rhode Island is \$314.94.) Variations in cost are due to type and quantity of service provided, labor costs and other factors.

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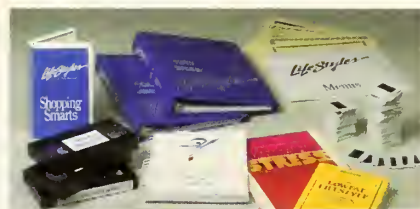
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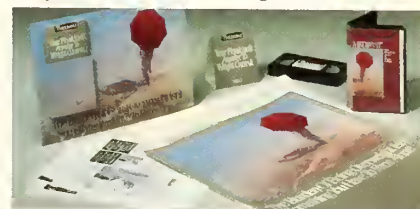
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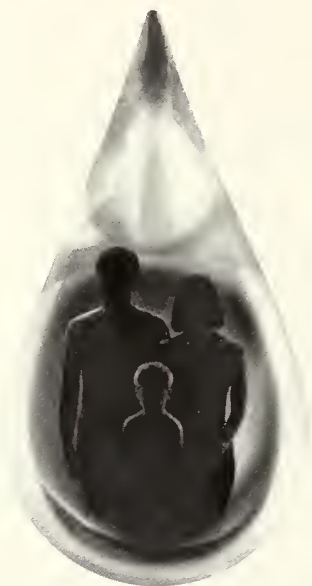


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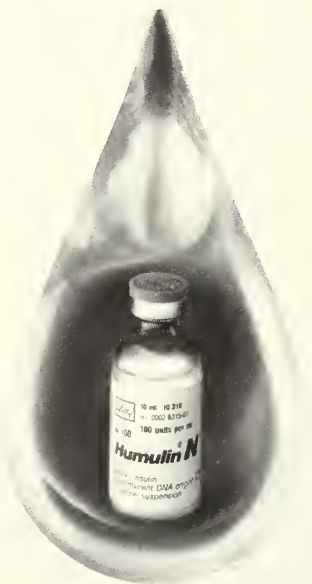
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PHYSICIANS IN THE NEWS

Doctor Mark E. Appleman has been appointed to the staff at Newport Hospital and has opened his practice in Infectious Diseases and Internal Medicine at Kings Grant Office Park, Portsmouth, Rhode Island. **Doctor Appleman** is Board Certified in both Internal Medicine and Infectious Diseases.

* * *

The Memorial Hospital of Rhode Island recently appointed **Doctor Samuel H. Greenblatt** as its Chief of Neurosurgery. He is also an associate professor in the Brown University Program in Neurosurgery. **Doctor Greenblatt** is certified by the American Board of Neurological Surgery and he is a Fellow of the American College of Surgeons.

Memorial Hospital of Rhode Island has appointed **Doctor Ronald Fischer** as its Anesthesiologist-in-Chief and Director of the School of Nurse Anesthesia.

Doctor Fischer is board certified in anesthesiology and pain management. He is a fellow of the American College of Chest Physicians, a member of the Society of Cardiovascular Anesthesiologists as well as other professional and international research societies and has published widely in the field of anesthesiology and pain management.

* * *

Doctor Richard V. Morgera has been appointed to the Newport Hospital Medical Staff as a full-

time Emergency Physician. **Doctor Morgera** is certified by the American Board of Internal Medicine.

* * *

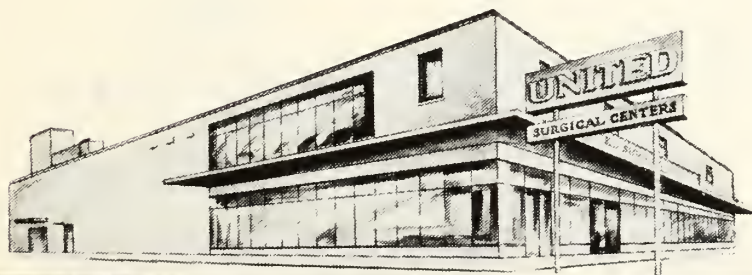
The United States Public Health Service presented **Doctor Patrick Dowling**, director of the Family Medicine Residency Program at Memorial Hospital of Rhode Island, with the "Regional Health Administrator's Award." The award is given to persons who have made an outstanding contribution in the field of public health in New England. The citation reads: "For your dedicated efforts in implementing the Community Health Center Model for training Family Practice Residences in Rhode Island."

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BOOK REVIEW

Psychiatry

Moments of Engagement: Intimate Psychotherapy in a Technological Age. Peter D. Kramer, MD. 260 p. New York, W.W. Norton, 1989. \$24.95

Slowly savoring my way through this book, not to be read at one sitting, it suddenly dawned on me why it was so engaging. With the basic theme that motivation, learning, experience, theory and practice are all flowing towards the endlessly repeated, yet forever unique encounter between patient and physician, the book was asking me where my moment of engagement with its inner life was. The answer clicked when I listened to the author reading some chapters aloud to a small, ever more engaged audience. Here was someone who had the irresistible drive, the pleasure and the dread, the courage to be an actor and observer at the same time and to want to let the world know about it. About himself.

To do this, Dr Peter Kramer had by necessity to use the medium of the word. To face the daunting challenge of writing what? Science? Literature? He says: "This is a book of stories," with the intent of trying — and succeeding with erudition and exquisite sensitivity — to ask the right questions and bring some clarity and understanding to the fledgling, the struggling art and science of psychiatry. To be read with great benefit by the specialist, the student and the educated layman alike.

What a task, being scientist, healer and artist all at once! Precedents are discouraging. The deepest understanding of the fullness of life, of happiness and suffering, has been derived from the unfathomable genius of great

writers. Sophocles, Dante, Shakespeare, Goethe, Dostoyevski, Flaubert, Proust, — so many more. How pale and arid do the valiant attempts at psychological, sociological, anthropological conceptualization and classification seem in comparison. Some have tried before to combine it all. To name just a few: Chekhov and William Carlos Williams practiced medicine and wrote unrelated literature; Somerset Maugham gave medicine up altogether; Joyce didn't make it through medical school. Robert Coles, John Mack, Robert Lifton, in our time, labor in the vineyard.

How does Peter Kramer do? Bravely, skillfully, — engagingly. The writer carries you along the journey of the exponentially rapid changes to which a young psychiatrist has to adjust in the field. It honestly brings alive the bewilderment in the face of ambiguities and complexities and the integrity needed to do the hard work of arriving at your own conclusions, on "chartless terrain." The need to use professional language at times gets unavoidably in the way of the narrative flow. There are nuggets of style: "The Gordian knot unties itself." Keep looking as you read. "For many concepts, the thing is just what we know it to be. If the definition fails, it is the definition which has failed, not the elusive concept." This, for example, makes it possible to convincingly define psychotherapy as undefinable. For being a "soft science" psychiatry is therefore the more demanding than those specialties with safe yardsticks and guidelines. While Peter Kramer is not afraid to show where his heart is, he is aware

and conscientious enough to use his head to compensate for it.

I do have one bone to pick. The moment Dr Kramer hears a patient talk about Rilke, he "feels the strong urge to put her on Tegretol®." Does this seem to indicate that a whole generation of my European contemporaries, who worshiped Rainer Maria Rilke, was afflicted with temporal lobe epilepsy?

This book is a breath of fresh air to help dispel the glut of misunderstanding that blurs psychiatry in the professional and the public mind. As literature it is a tantalizing promise. Will it be humanly possible, as the years go by, for the author to achieve the leisure, the distance, the complete absorption in the agony of writing, that would make it possible to look forward to the masterwork yet to be written in this genre?

Hugo Taussig, MD



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Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause granulocytopenia at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: **General Impaired Renal Function:** As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

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Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radioactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that

show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not been clearly defined, VASOTEC[®] (Enalapril Maleate, MSD) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome: Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypertension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of ¹⁴C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2987 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were: headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were: dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were: fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), angina pectoris (1.5%), nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring since the drug was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients. (See WARNINGS, Hypotension.) Cardiac arrest, pulmonary embolism and infarction, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis or cholestatic jaundice, melena, anorexia, dyspepsia, constipation, glossitis, stomatitis.

Musculoskeletal: Muscle cramps.

Nervous/Psychiatric: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction. (See PRECAUTIONS and DOSAGE AND ADMINISTRATION.)

Respiratory: Bronchospasm, rhinitis, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Herpes zoster, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, tinnitus.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgia, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 11% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: **Hypertension:** In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed.

If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium. (See PRECAUTIONS.)

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance >30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure who have hyponatremia (serum sodium <130 mEq/L) or with serum creatinine >1.6 mg/dL, therapy should be initiated at 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d., then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more, if at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function. The maximum daily dose is 40 mg.

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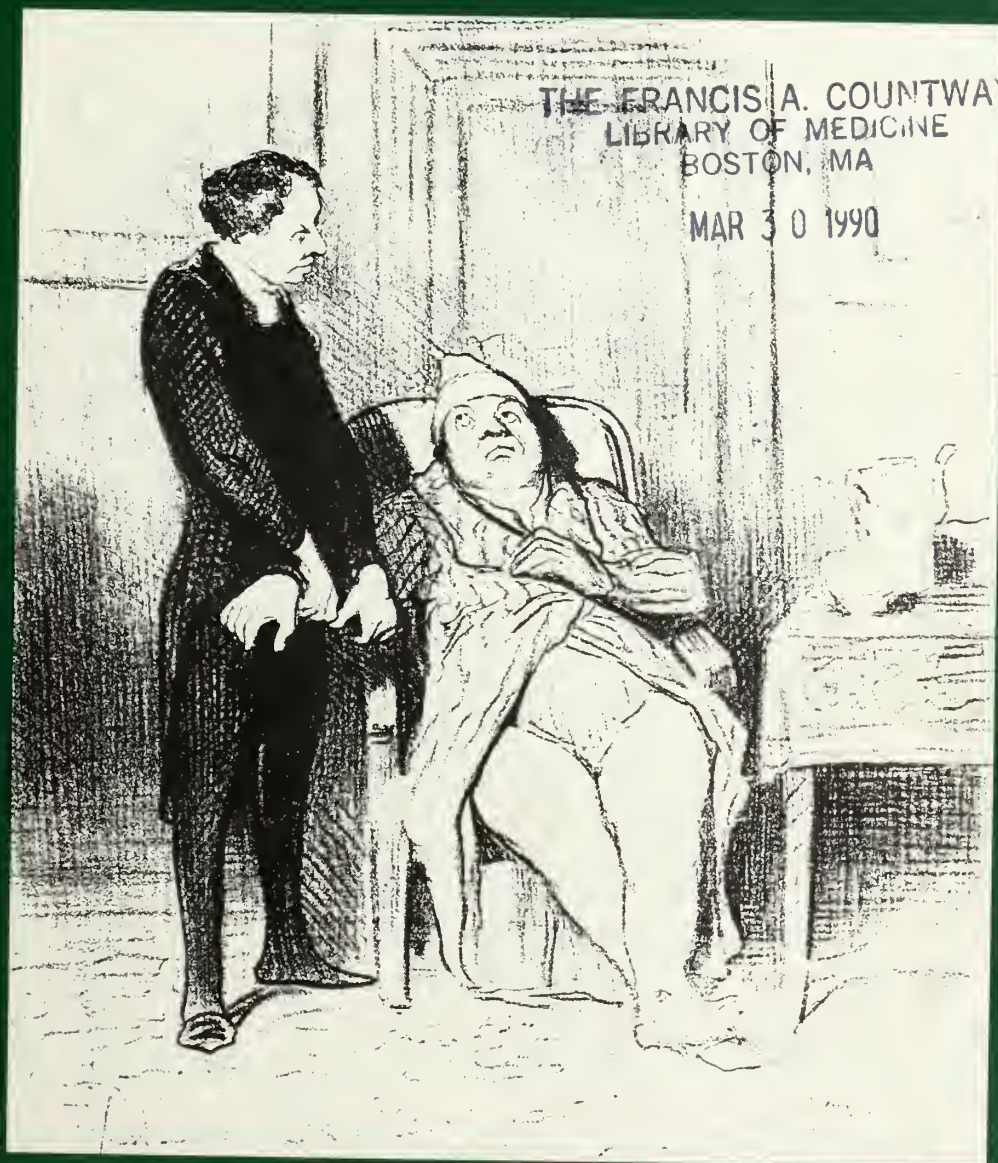


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March 1990

Volume 73, Number 3



*Clinical Observations
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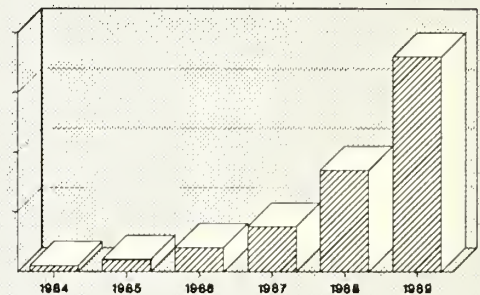


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Cover: A lithograph by Honoré Daumier entitled "Ah! docteur . . ." published in *le Charivari*, October 19, 1847. The translation reads "Doctor, I believe I'm consumptive."

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Clinical Observations in Rhode Island

This issue of the *Journal* contains five papers representing the diverse observations, speculations and recommendations of practicing physicians in Rhode Island. The described clinical phenomena range from the common (post-tonsillectomy bleeding) to the bizarre (self-enucleation) but all are part of the authentic fabric of Rhode Island medicine. The Publications Committee which supervises the direction and philosophy of this *Journal* has determined that about two out of every three future issues shall be dedicated to a single subject such as AIDS or health problems in Rhode Island tourists; but they also recognized and hoped to exploit the rich and varied bedside experience of the many practitioners, academicians and house staff in Rhode Island; accordingly, they assigned about one-third of the *Journal* issues to unsolicited papers of practical medical interest. The Committee and the Editors of the *Journal* encourage the readers to submit brief clinical papers for possible publication. And while we hope that an extensive literature search accompanies the preparation and writing of each of these contributions, a lengthy historic background within the text is not necessary. Each issue of the *Journal* contains a page entitled, "Information for Authors." We hope that each potential author will review

these instructions with the care that they deserve before submitting his or her manuscript.

The Editors

The Critical Eye of Honoré Daumier

The France of the nineteenth century which had nurtured luminous medical scientists such as Claude Bernard, Charcot and Laennec also produced a number of gifted artists who had employed their graphic talents in portraying the darker side of medicine. Preeminent amongst these was Honoré Daumier, whose lithographic art was in the social-commentary tradition of England's Hogarth and Spain's Goya. Daumier, like his countryman Molière, often portrayed physicians as pompous yet mediocre simpletons, dangerously uneducated, lacking in any scholarly concerns, insensitive and venerating but money and status. Physicians, in Daumier's words, were "... all profiteers, mouthers of garrulous clichés and mountebanks." Who was this cartoonist and occasional sculptor with such assertively caustic views?

Daumier was born in 1808 into a Marseilles working-class family. As a child he was described as discontented, melancholic and with a macabre humor. He expressed a bitter and febrile hatred for the established classes, par-

ticularly the tyrannical and "philistine bourgeoisie." He demonstrated substantial graphic talents as an adolescent and received a modest measure of formal training in the arts. His professional life was devoted, in essence, to caricatures, some four thousand of which were published in the Parisian magazines *le Charivari* and *la Caricature*. The bulk of his adult artwork portrays lawyers, physicians, the judiciary, the police and the merchant class in an uncharitable light. Once during his earlier career an unfavorable cartoon of Louis Phillipe actually resulted in a six-month prison term.

Daumier enjoyed good health through most of his life and rarely needed the services of a physician until his final illness in 1878 which rendered him totally blind. He lived most of his life at the margins of poverty and died in a small cottage on the banks of the Oise river, in a home provided for him through the generosity of the artist, Corot.

It is surprising that the art of Daumier, which depicts medicine in such unmerciful terms, is so universally appealing to physicians. There are many practitioners' offices with a cherished Daumier lithograph proudly and prominently displayed on some wall. Indeed, an excellent Daumier print enlivens the Rhode Island Medical Society's library. In honoring Daumier perhaps we are appreciating great social art; perhaps we are acknowledging that these drawings are accurate com-

mentaries of the medicine of 150 years ago; and perhaps, too, we are now strong enough to laugh at our own foibles.

The cover illustration of this month's *Journal* is an 1847 Daumier print entitled, "Ah! docteur." Next month's issue, which will be devoted to articles on medical quackery, will also have a Daumier print enriching its cover.

Stanley M. Aronson, MD

Botany and Medicine

This is the time of year when seed catalogs mix congenially with medical journals in the morning mail. It is the season when growing things become more than a distant recollection, when there is a breeding of lilacs "out of the dead land, mixing memory and desire, stirring dull roots with spring rain." Medicine and botany seem far removed from each other in pace and purpose; yet there was a time in the history of medicine when the distance between the herbal garden and the sick-room was quite short. Many of the botanically based apothecary arts of yesterday have blossomed into the medical sciences of today. Both are concerned with life and growth and the ancient union between medicine and botany persists.

Medicine readily acknowledges the many contributions that botanists have made to pharmacology. There is an equally rich body of contributions made by physicians to the science of botany which is not as prominently recorded. Many of these physician-naturalists are not currently well known within the medical profession and it is therefore worth reviewing their scientific efforts in both fields.

Leonhard Fuchs, a Bavarian born in 1501, received his medical degree from the University of Ingolstadt and ultimately was named the professor of medicine at Tübingen University. His great interest was in botanical therapeutics and he was responsible for one of the first published descriptions of the physiologic actions of the plant, foxglove (*digitalis*).

Matthias de Lobel, a sixteenth century native of Lille, emigrated to England in 1564 and rose to become physician to the court of James I. He divided his scientific interests between medicine and the classification of native plants of England and the low countries.

Pierre Magnol, born in 1638, and eventually the professor of medicine at Montpellier University, was France's leading botanist of the seventeenth century.

George Joseph Camellus, a seventeenth century Moravian Jesuit, was skilled in both botany and medicine. He spent his adult years in the Far East, particularly the Philippines, as a missionary. He systematically described the flora of the Far East and his botanical journals formed the basis of later horticultural texts.

Olaf Rudbeck was one of Sweden's most illustrious physician-naturalists and a teacher of Carl Linnaeus.

Carolus Linnaeus was born in southern Sweden in 1707 and studied medicine at the prestigious Upsala University. While completing his training for his medical degree he assembled his first major botanical text under the guidance of Celsius, the monumental work entitled (translated from the Latin), "*Preliminaries on the marriage of plants, in which the physiology of them is explained, sex shown, method of generation disclosed, and the true analogy of plants with animals*

concluded." During his lifetime, Linnaeus maintained an active practice of medicine while holding the chair in Botany at Upsala University. He initiated the binomial classification system for both plants and animals.

Anders Dahl was a medical student of Linnaeus who devoted most of his brief life to the study of native plants.

Caspar Wistar was born in Philadelphia in 1761 and received his medical degree from the University of Edinburgh. He joined the faculty of the first medical school in the colonies, the University of Pennsylvania, authored the first American text in anatomy, founded a museum of natural history in Philadelphia (later to be called the Wistar Institute) and was one of the leading scholars and philosophers of his native city.

Joel R. Poinsett was born in South Carolina in the year 1779. He attended Edinburgh medical school but never actively practiced medicine. Rather, he entered politics, was James Madison's roving ambassador to South America, a member of Congress and a Secretary of War in Van Buren's cabinet. During all of these crowded years he maintained an active interest in horticulture particularly during his extensive travels throughout Central and South America.

With the exception of Linnaeus, few of these physicians are remembered in the formal annals of medicine. And yet we lovingly preserve their names — and their many contributions to botany and to medicine — each time we admire **fuschias, lobelias, magnolias, camellias, rudbeckias, dahlias, wisterias**, and at yuletide, **poinsettias**.

Stanley M. Aronson, MD

EDITOR'S MAILBOX

Detoxification of the Chemically Dependent Patient

I was pleased to see your informative review article on detoxification in the *Rhode Island Medical Journal*. However, I feel the medical public should be made aware of the appalling inadequacy of detoxification programs in Rhode Island. As Director of Rhode Island Hospital Emergency Department, I am aware of the refusal of detoxification services to an average of three or four patients each day. These patients can not afford private detoxifica-

tion programs, do not have health insurance and can not go to the State's Substance Abuse Unit or Providence's social setting Detoxification Center because of overcrowding at those facilities.

At a recent meeting of the Hospital Association of Rhode Island (HARI) Committee on Emergency Medical Services, it was estimated that only one half of the patients presenting to RI Emergency Departments with acute intoxication can be accommodated

in existing programs due to the lack of beds. While the medical management of acute detoxification is expertly outlined in your article, the *real* crisis of providing resources for patients who need acute detoxification must be addressed.

Robert H. Woolard, MD
Director/Department of
Emergency Medicine



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Resident Report: A Conference With Many Uses

Fred J. Schiffman, MD
Michael F. Mayo-Smith, MD
Melvin D. Burton, MD

"To emphasize (the need for brevity of presentation) we ask that the case be presented as though the house officer were calling from Seattle to a consultant in New York and paying for the phone call himself."

Although the origins of Resident Report (RR) are somewhat obscure, its place is now well established in many teaching hospitals. In order to learn how various internal medicine programs conducted RR, we designed a questionnaire and sent it to members of the Association of Program Directors in Internal Medicine at 412 hospitals.

There have been several recent articles concerning the conduct of RR. A paper by Gibbons¹ is a

provocative account of RR at a military hospital. Another article, appearing more recently, was based upon a questionnaire sent to 124 Departments of Medicine represented by the membership of the Association of Professors of Medicine.² Our study differs from the previous two in that it examines RR in the context of a survey sent to a variety of teaching hospitals throughout the United States including community, municipal, university, Veteran's Administration, and military hospitals.

Methods

A questionnaire was sent to 412 United States internal medicine program directors based upon a list obtained from the Association of Program Directors in Internal Medicine. The questionnaire, containing forty items requiring a response in the form of multiple choice answers or comments, was sent on September 11, 1985 and returns were accepted until January 30, 1986. Two hundred and eighty-six questionnaires were returned for a response rate of 70 percent. No follow-up calls or letters were sent to those who did not respond by January 30,

1986, an acknowledged potential source of bias. While characteristics of the hospitals which did not return the questionnaire were similar to those that did, it was still possible that certain features of this group (which equalled 30 percent) could have changed the analysis of our information. Each question was analyzed based upon the number of institutions responding to that individual question. Where no response was made to an individual question, it is so indicated in the analysis of data presented below.

The questionnaires were filled out by the Chief of Medicine, the Director of Medical Education, Program Director or Chief Resident, at the discretion of the individual program.

Results and Discussion

Time and Frequency

All respondents indicated that they conducted RR of some type.

ABBREVIATIONS USED:

AFB: Acid-fast bacilli

CBC: Complete blood count

PGY-I: Post-graduate year one

RR: Resident report

Fred J. Schiffman, MD, is Associate Professor of Medicine with Brown University Program in Medicine/The Miriam Hospital, Providence, Rhode Island.

Michael F. Mayo-Smith, MD, is Clinical Instructor in Medicine with Harvard Medical School, Boston, MA and VA Medical Center, Manchester, New Hampshire.

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RR was held most often in the morning (97 percent) in a conference room adjacent to Department of Medicine offices; 72 percent began before 9:15 am. An hour was the most common length of time of the conference. As shown in Figure 1, 38 percent of hospitals responding held RR seven days a week. Twenty-nine percent of hospitals conducted report five days a week, 13 percent conducted RR four and 13 percent six days a week. Only 6 percent of hospitals conducted RR three or fewer days a week. Almost 80 percent of responding programs indicated that report was conducted five days a week or more. Sunday was the most frequently eliminated day.

While there are some authors who feel that RR is best held in the early morning as the "maiden event of the day,"¹³ there are others who believe that work rounds should precede RR, especially since data from work rounds can be added to information gleaned from the residents' morning evaluation of the patient, and makes the discussion at report as timely as possible. Our questionnaire did not determine whether RR was held before or after work rounds but 46 percent started RR by 8:00 am and 72 percent by 9:00 am. We also assume that RR most often preceded ward attending rounds, given the time slot of RR. Only a small percentage of programs (4 percent) conducted RR in the afternoon. There may be some advantage to holding RR following ward rounds, since the ward attending physician may feel that his role is usurped by the discussion which has already taken place at RR and that the ward attending physician's input might be valuable for discussion at RR.

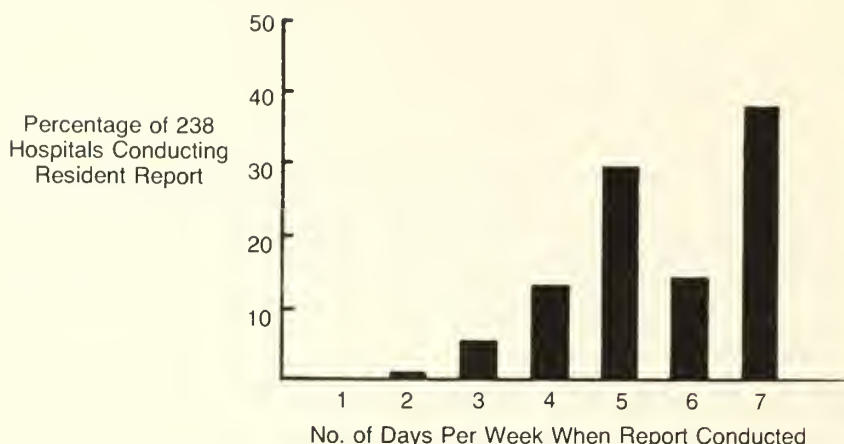


Figure 1. The percentage of 238 hospitals conducting resident report from one to seven days per week.

Participants, Leadership & Tone

Attending physicians who attended RR on a regular basis included the Chief of Medicine more than 60 percent of the time, and the Director of Medical Education approximately 50 percent of the time. Seventy-two percent of hospitals responded by indicating that other attending physicians were permanently assigned to RR duty at 15 percent of the hospitals responding. At approximately 50 percent of the hospitals, attending physicians were on a rotating schedule and at approximately 25 percent of hospitals, attending physicians dropped in on a casual basis. The Chief Medical Resident was present at RR at 90 percent of the hospitals which responded. Interns (PGY-1s) were present at RR in 58 percent of the hospitals polled. Ninety-six percent of the programs included PGY-2s on a regular basis and PGY-3s were present in 89 percent of the programs responding. The residents who attended were most commonly assigned to ward or intensive care unit rotations. However, in many of the programs, residents who were in the

emergency room or on elective also attended.

Other individuals who might attend report included ER physicians, fellows, students, librarians, nurses, pharmacists, and pathologists. Most of the hospitals which responded indicated that guest participation was encouraged (70 percent of the time).

The Chief Resident exerted a major leadership role in 64 percent of responding programs. Forty-six percent of hospitals indicated that the Chief Resident alone ran RR but other contributors included the Chief of Medicine or designated attending physicians. In 51 percent of the sample, the Chief Resident played a major role in setting the tone of report either alone (30 percent of the time) or in combination with other participants (21 percent of the time). Once again, the Chief of Medicine played a major role in 26 percent of responding programs. The atmosphere was characterized as "loose" by 74 percent of responding hospital programs, "rigid" by 10 percent, and a combination of loose and rigid in 14 percent of 286 pro-

grams. Other adjectives were used to describe the atmosphere by 3 percent of respondents.

As noted above, 60 percent of responding hospitals indicated that the Chief of Medicine participated at RR on a regular basis. This participation is felt to be critical for several reasons. Since RR is an important mechanism which permits the service chief to monitor many aspects of clinical care in his or her hospital, and learn about the strengths and weaknesses of the staff in dealing with newly admitted patients, our belief is that the Chief should not be substituted for by anyone else. In a recent survey, 19 percent of respondents, all of whom were identified as Department Chairs, indicated that the purpose of morning report was to "... allow the Chief of Medicine or Program Director to keep tabs on the medical service." And another 21 percent believed that morning report served principally to "... review management decisions, including bad outcomes."² Aside from this quality control issue, the Chief's presence gives a valid impression of interest and involvement on the part of this primary role model for house staff. Also, it allows the Chief to directly infuse his or her own approaches to patient management in a variety of patient care settings presented to the RR group. No less important than the medical, diagnostic and therapeutic skills proffered are the moral and attitudinal tones set by the Chief. As noted above, the Chief of Medicine did exert a major leadership role and set the tone in many hospitals. Several programs indicated that they felt their RR was special because of the high degree of involvement of the Chief of Medicine, inferring that such involvement was not universal, and that no surrogate could bring the same aura to RR.

While many programs indicated that there were a large number of participants at their RR, and guest participation was encouraged by 70 percent, it is our experience that a *smaller* "cast of characters" often allows the best teaching to occur. While the presence of subspecialists and ancillary medical personnel often provides instantaneous answers and resources for discussion purposes, such participants' presence may interfere with the development of certain skills in medical residents: A good generalist must know how to approach a whole variety of medical and non-medical issues without the ready availability of consultants. While he or she may have access to textbooks and other medical literature (see below), the competent internist should be able to carry a problem to an advanced state of resolution. While the presence of a large number of experts makes knowledge acquisition easy, it often does not allow residents the time and space for requisite meandering with, and percolation of, clinical data presented to them. In other words, clinical reasoning with its blind alleys and false passages can sometimes be inappropriately short-tracked; important decision pathways are foreshortened by many well-meaning but irrepressible consultants, in a way that makes learning suboptimal.

Additionally, a large number of participants detract from the "clubby" atmosphere. This atmosphere should not necessarily be seen as elitist. It allows for a relaxed and intimate interaction between participants. Residents are more likely to admit their own ignorance, constructively criticize each other, and show off less, where the audience is small. Besides, it fosters more frequent participation by each of the residents present and allows the Chief

of Medicine and the Chief Resident to more fully evaluate the participants. The Chief may also be more open and self-effacing with a small group (and his or her own foibles more easily revealed). Such revelation is also important since it proves that even "the Chief" has gaps in knowledge, and idiosyncracies which the house staff can more easily know (and criticize) in a more private forum. As noted below, the methods by which a senior clinician responds to criticism and improves and acquires his or her information is an important lesson in itself.

Residents are more likely to admit their own ignorance, constructively criticize each other, and show off less, when the audience is small.

The presence of interns at report may be inhibiting to more senior residents (see above). Also, problems specific to PGY-1s may not be discussed by the group of residents who must supervise them. Our own program does not encourage PGY-1 participation. Exclusion of PGY-1 residents may add to the undeserved mystique with which RR is associated, but it also simplifies the number of educational levels which must be addressed by the leaders of RR. While other conferences, including ward attending rounds, involve medical students, sub-interns, interns, and residents, these sessions are much less efficient at transmitting certain medical lessons economically to this "one-room schoolhouse group" than in a forum where the educational background is approximately the same. RR with only PGY-2s and 3s thus becomes a high level and special conference.

Some programs allow PGY-1 participation in the second half

of the year and still others allow interns to come one or two days a week and these seem like reasonable approaches. Our program has a special interns' report one day a week with the Chief of Medicine.

If pathologists and radiologists, as well as the other participants noted, are present at RR, how does it differ from attending rounds or other subspecialty conferences? Perhaps it is that spontaneous thoughts are generated, and one gets to see how clinicians deal with data presented to them, especially if presented in the same way it came to the residents.

Patient Presentations

Almost exclusively, residents who worked up the patients presented them. The Chief Resident and the residents themselves selected patients to be presented most of the time.

Twenty-three percent of respondents indicated that 91-100 percent of admitted patients were presented at RR. However, the absolute number and percentage of admissions which were presented varied widely (see Figures 2A, 2B), most commonly two to four patients were presented. The most common time period allotted for presentation of individual patients was less than five minutes in 45 percent of responding programs. Five to ten minutes was the time allotted by 30 percent of hospitals which responded, 12.5 to 25 minutes by 10 percent of the programs which responded with a numerical assessment of time for presentation. Other programs either did not respond to this question (4 percent) or used adjectives such as "brief," "succinct," and "complete" to describe the length of time for presentation (12 percent).

Patients were presented from memory by 19 percent of re-

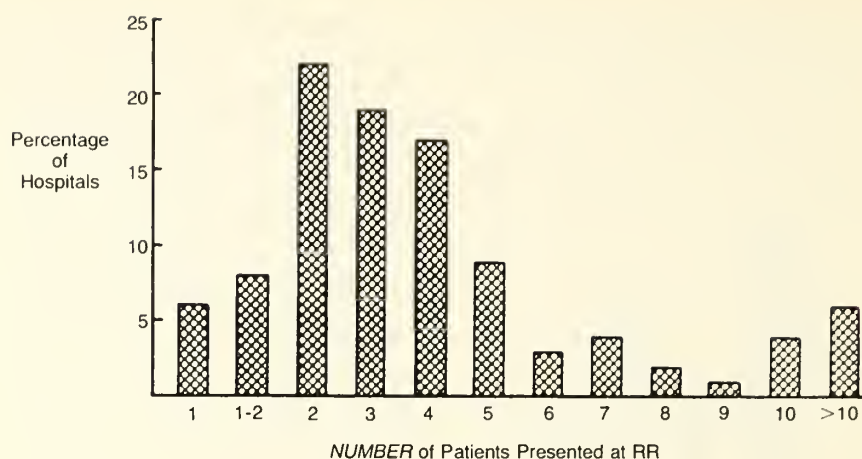


Figure 2A. Percentage of hospitals where the indicated number of patients were presented at Resident Report. Number of responding hospitals was 247.

spondents. Over eighty percent of the time, presentation aids such as xerographic copies of write-ups, index cards, or the write-ups themselves were used by residents. There was no correlation between the type of program (eg, University, Veterans Hospital, military hospital) with the use of presentation aids. Interruptions were tolerated or encouraged by 75 percent of programs which responded.

One of the more colorful descriptions in the literature (and repeated by one of the questionnaire respondents) regarding the need for brevity of presentation was "... to emphasize this point we ask that the case be presented as though the house officer were calling from Seattle to a consultant in New York, and paying for the phone call himself!"¹

While we did not ask about this specifically, we believe that the format of RR at any institution will vary throughout the year. First of all, depending upon the experience and skills of the participating residents, the Chief Resident is required to place appropriate emphasis on educational content and technique. In July, certain basic diagnostic and therapeutic information must be stressed,

while later in the year, emphasis may be placed on the more subtle aspects of patient care. Similarly, it may be necessary for all admitted patients to be briefly presented during the first part of the year in order that appropriate comment be made about the widest range of problems. During the middle of the year, it may be most appropriate for the Chief Resident to then select cases to be presented and discussed, guided in part by the background of the specific cohort of residents then at RR. In the latter half of the year, the residents themselves can be given the opportunity to select the cases to be presented and these would be discussed in some depth. Pupa and Carpenter have described a dynamic and successful morning report format which utilizes several effective techniques.⁴ These include "... an internal monitoring system to guide case selection, pre-conference preparation to delineate major teaching points, timely follow-up of previously described cases, and generation of a pertinent bibliography. ..."

Residents usually learn to present cases in such a fashion that they can direct discussion or provoke responses from RR partici-

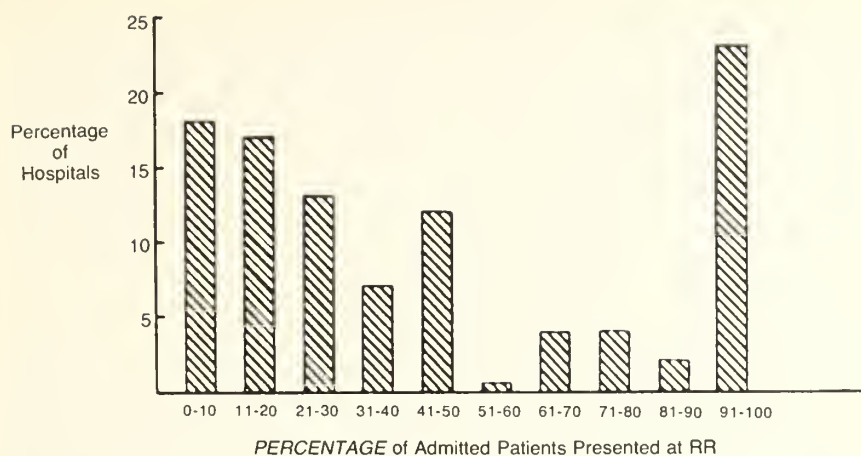


Figure 2B. Percentage of hospitals where the indicated percentage of admitted patients were presented at Report. Number of responding hospitals was 248.

pants. One successful approach has been to allow residents to present the information as they learned it rather than the traditional history, physical, laboratory data sequence, in order to more accurately recreate the scenario with which they were involved as the patient was admitted. Key pieces of information may be withheld and thus reproduce the dilemmas of the night before. This technique encourages other residents to participate in a realistically reconstructed patient care problem. If the denouement is temporarily delayed by the presenting resident and all RR participants encouraged to give their opinion about what-they-would-have-done-if-they-were-there, this gambit often results in an interesting array of diagnostic and therapeutic responses. Many such responses may bear no resemblance to what was actually done, but they well illustrate that there is often no single correct answer and that there is no substitute for being there and dealing with the patient directly.

It is often interesting to observe the vociferousness of opinion-stating by those not directly involved with a given patient and

also the gratuitous commentary made about the level of care by other physicians not present at RR. Such harsh criticism is a potentially pernicious aspect of RR and often requires a strong leader to appropriately curtail. Especially effective in this regard is follow-up information for the group: when more complete information from the initial encounter, or full outcome data are provided to the RR group at subsequent sessions, a seemingly absurd approach (which had elicited harsh criticism initially) may now be looked upon as quite sensible.

Another effective reality-testing technique involves traveling to the bedside to verify historical points or physical exam information. As has been shown by others, this can be a humbling experience for the resident presenting the case since the data obtained by the group often bear little resemblance to what was presented.^{5, 6} In our survey, the group of RR participants at 33 percent of responding hospitals went to the bedside to observe or verify historical or physical finding data. Some programs actually had patients brought to report, and in our own hospital we have found that certain easily demonstrated

physical findings in ambulatory patients are most easily viewed when the patient is brought for a brief appearance at RR (however, this happens rarely). To enliven RR, pathologic specimens (gallstones which occluded a common bile duct and which were imaged by an ultrasound study presented the previous day, or the actual impacted food bolus previously seen only in shadow form on a ciné esophagram) are especially effective.

Recordkeeping

Twenty-three percent of respondents indicated that no form of recordkeeping was used during RR. Forty-one percent of the time a logbook was the method of choice to record patient information (most frequently including patient name, unit number, diagnosis, and pertinent historical, physical and laboratory data). Other forms of recordkeeping were also used, including a chalkboard and a computer.

It is our opinion that the recording of pertinent data about patients who were presented at RR is of importance for several reasons: 1) It allows more than desultory follow-up of patients who were previously presented. 2) The record of problems which were discussed in depth at report allows the Chief Resident and Chief of Medicine to make certain that a wide variety of problems is covered during the course of a resident's participation at report. 3) It serves as a repository for information which can be the basis for other teaching conferences such as Grand Rounds, CPCs, Patient Management, or Morbidity & Mortality Conferences. 4) Recording the name of the responsible residents and attending physicians allows the Chief of Medicine to review patient management from a quality assurance perspective (and some accredi-

tation agencies actually require that such review be documented). 5) While there is often sampling error, certain trends in diagnosis frequency and disease frequency may become highlighted. 6) Recording of physical diagnosis data allows the Chief Resident to select appropriate cases for physical diagnosis tutors. 7) Timely follow-up can be given to Emergency Room or other health care personnel who are involved in the initial evaluation and therapy of patients. It is of interest that of the 23 percent of respondents who indicated that no form of recordkeeping was used, most of these programs did allow regular time for follow-up. This may have been more completely done if a form of recordkeeping were available.

Food and Drink

Food and drink were provided by 61 percent of the questionnaire respondents. Most often this consisted of coffee and tea but the range of foods was broad (donuts, bagels, pastry, fruit juices) and, in some cases, included full breakfasts, while in others residents were allowed to bring food to the conference but it was not provided for them. Most often hospitals which had a "loose" report served food and/or drink. And most often programs which considered themselves "rigid" did not.

Educational Tools

Textbooks were used by RR participants in 20 percent of responding programs. Xerographic copies of journal articles were provided 72 percent of the time by RR participants. Residents gave brief talks on a subject assigned by the report leader in 63 percent of the programs which responded.

Textbook use is felt to be an extremely valuable exercise dur-

ing RR, especially when a more senior clinician uses such texts as part of the discussion of a patient. We maintain a core internal medicine library (the one suggested by the American Board of Internal Medicine⁷) in the room used for RR. When there is an issue which is questioned or controversial, rather than defer the answer until someone looks it up for the next day's session, almost always we can provide the needed data by using one of the core textbooks. Such use by attending physicians in a natural and frequent way, reinforces the notion that one can not be expected to know everything and that use of textbooks should be an easy and comfortable action during the course of patient care. Other programs use a computer linked to the National Library of Medicine or other literature repository, for instantaneous availability of up to date medical literature data. Some programs even had brief journal clubs in the context of RR. The presence of a medical librarian was a feature of which some programs felt proud. Our own experience is that, while this can occasionally be a resource,⁸ this additional person will add to the audience and overall formality, and may inhibit the free and easy dialogue between residents and the report leaders. Our residents have easy access to our clinical librarian and requests for medical literature are talked about with her after RR is completed.

Non-Medical Issues

While specific house staff problems were discussed by only 56 percent of RR questionnaire respondents, many who did carry on such discourse felt it was an extremely valuable part of RR. Difficulties with the admitting system or with particular medical personnel were often best dealt with in the presence of the Chief

of Medicine and Chief Resident who might aid in or expedite the solution of such problems. At 85 percent of responding hospitals, non-medical issues were discussed and included social, personal, ethical, political, and medical economics topics.

Follow-up

Regular follow-up of selected cases occurred at 174 of 286 RR

When follow-up did not occur on a regular basis at RR, other conferences such as Pathology, Morbidity & Mortality, and Patient Management conferences were found to be alternatives where outcome data could be provided.

surveyed (61 percent). Such follow-up occurred at the beginning of RR in 26 percent, at the end in 35 percent, and "sometimes at morning report" in 39 percent of programs responding. In only 3 percent of the programs surveyed was no follow-up time provided on a regular basis. Follow-up was provided to the ER physician who made initial contact with the admitted patient in 75 percent of programs surveyed.

Where follow-up did not occur on a regular basis at RR, other conferences such as Pathology, Morbidity & Mortality, and Patient Management conferences were found to be alternatives where outcome data could be provided.

Data Used and Special Features

The group of RR participants at 33 percent of responding hospitals went to the bedside to observe or verify historical or physical examination data. Ninety-four percent of responding programs indicated that x-rays, ECGs, microscopic slides, etc, were used

by participants during RR. Eighty-nine percent of responding programs indicated that educational, clinical, or research efforts were stimulated by RR.

When asked what was considered special about their RR, responses included the following: "... conducted by the Chief Resident and resident as their conference. . .," "... report is not a review of all admissions, but rather an academic discussion of the most interesting cases. . .," "... report keeps the Chief of Medicine informed and involved with house officer activities. . .," "... this is a business session, not a casual social interaction, residents are expected to know patients thoroughly, to have read relevant material. . .," "... Chief Residents know cases in advance and review the text and literature prior to presentations." "Report focuses on a detailed review of a few cases. It is not for the Director of the Medical Residency or the Chief of Medicine, it is for residents."

Another program's report was special, it was felt, because "... the focus is clearly educational rather than intake." Yet other sessions were "... designed primarily for administrative review. . . ." Many respondents expressed the feeling that "this report is distinct from sign-in and sign-out conferences which serve a patient care function."

Other responses about the special aspects of RR included: "... the emphasis on clarifying medical reasoning. . .," and "... the focus on medical humanities. . .," with one program director reading from works by Lewis Thomas and William Carlos Williams.

The use of the Medical Knowledge Self-Assessment Program questions during each session, and the presence of pathologists, librarians, social workers, and

other personnel who "enriched" the group at RR, were considered special by some programs. Others commented upon the presence of subspecialists and specialists who provided instantaneous mini-consultations during RR. In other sessions, there was a review of gross pathologic specimens and/or organs from autopsies of patients presented at report previously.

There were some groups who felt that the "close knit small group of residents" was important for the optimal functioning of report. However, one program actually held report before an audience of thirty to sixty people.

RR was characterized by several programs as the "... prime nuts and bolts teaching session with good exposure of house staff to departmental leadership." Many questionnaires included comments which stressed the importance of the Chief of Medicine at RR sessions and that the regular participation by the Chief was what was most special about their RR.

The absence of interns in sessions where residents could feel comfortable about discussions of their mistakes and alternative modes of therapy, was mentioned by several respondents as a most special aspect of their RR. On the other hand, other respondents felt that the presence of interns during at least some of the RR sessions allowed them to learn the specialized lessons that RR had to teach at the earliest possible time.

One respondent commented that "... the pleasant non-judgmental atmosphere . . ." was what was special about their RR. On the other hand, another program director commented that "... questions are asked of the interns which really puts them in the hot seat. . . ."

We have used a video screen

linked by a camera to a microscope in order to demonstrate urinalyses, Gram and AFB stains as well as CBCs and bone marrows, where pertinent. However, we try not to let the more technical aspects of initial patient management dominate, and spend the bulk of time with clinical decision making, using available data.

One successful approach has been to allow residents to present the information as they learned it rather than the traditional history, physical, laboratory data sequence, in order to more accurately recreate the scenario with which they were involved as the patient was admitted.

Conclusions

A major goal of RR (as with the training program in general) is to teach residents how to act upon available medical data in the most cogent and humane fashion, and when and how to acquire further information. Very often residents will stop during the course of their presentation and ask one of their colleagues what he or she would do with the information thus far presented. Attending physicians, including the Chief Resident and Chief of Medicine, are similarly examined, initially by only the more emboldened residents but this "table turning" becomes much less of a daunting phenomenon as the year progresses and as the true collegial intent of RR becomes apparent.

The utility of RR did not end with a given session, judging by 89 percent of respondents. Educational, clinical or research efforts were stimulated by RR according to these programs. As noted earlier, careful recordkeeping fosters development of edu-

cational programs and can serve as the basis for demographic or epidemiologic studies. In addition, research projects can be stimulated by RR and several publications by our own residents have resulted from interests generated at RR.

From our own experience, and what is written in the medical literature, as well as from the results of our questionnaire, it is clear that RR can be an exciting and enriching conference for house officer and attending physician participants, being tailored to individual or group needs. While, at times, it may seem that the many agendas that must be satisfied are mutually exclusive, sensitive leadership and guidance at RR can often accomodate both the desires of the house staff to learn from their initial experi-

ences with the patient they present, and the wishes of the faculty to affect management and exert quality control in the day-to-day care of patients.

This is a conference with many purposes, performed in a variety of ways by different hospitals. With appropriate guidance, both educational and patient care goals can be satisfied.

References

- ¹ Gibbons RB. Design for a successful morning report. *Military Medicine* 1982;147:578-79.
- ² Parrino TA, Villaneuve AG. The principles and practice of morning report. *J Am Med Assoc* 1986;256:730-33.
- ³ Sivaprasad R, Tagushi JT. Starting the day right at a teaching hospital. *Am Col Phys Observer* 1982;2:1-2.
- ⁴ Pupa LE, Carpenter JL. Morning report: A successful format. *Arch Intern Med* 1985;145:897-99.
- ⁵ Linfors EW, Neelon FA. The case for bedside rounds. *New Eng J Med* 1980;303:1230-33.
- ⁶ Wiener S, Nathanson M. Physical examina-

tion: frequently observed errors. *J Am Med Assoc* 1976;236:852-55.

⁷ Lewis CS. A library for internists V. *Ann Intern Med* 1985;102:423-37.

⁸ Barbour GL, Young MN. Morning report: role of the clinical librarian. *J Am Med Assoc* 1986;255:1921-22.

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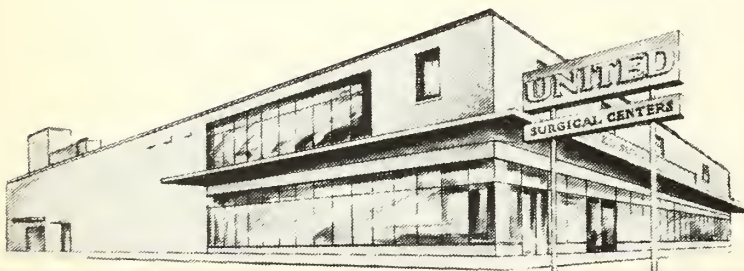
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Predicting Bleeding in Common Ear, Nose, and Throat Procedures: A Prospective Study

Peter S. Smith, MD
Paul J. Orchard, MD
Mary D. Lekas, MD

Our data do show . . . that abnormalities of two of the laboratory tests, the aPTT and SBT, indicate a greater risk, notwithstanding our inability to establish a specific diagnosis in some.

Tonsillectomy, adenoidectomy, and myringotomy with insertion of ventilating tubes are the most common surgical procedures performed in children and young adults.¹ The predominant risk associated with these procedures is hemorrhage, particularly following tonsillectomy.²⁻¹¹ The inci-

dence of postoperative bleeding varies, with some authors reporting a rate as low as one percent, and others as high as ten percent.⁷ Discrepancies may be due to several factors, including the routine use of aspirin-containing chewing gum prior to the mid-1950s, differing surgical techniques, as well as differing definitions of what constitutes significant bleeding. The mortality reported with tonsillectomies also varies, from none⁸ to 2/10,000.¹⁰

Two categories of postoperative hemorrhage which occur with similar frequency are distinguished in the literature.³⁻⁴ Primary, or reactive, bleeding takes place within 24 hours of surgery and is often attributed to surgical technique or a hemostatic disorder.³ Secondary bleeding, occurring up to 14 days after the operation and of uncertain etiology, often coincides with sloughing of the surgical eschar. Excessive bleeding may result from a disorder of platelet/vessel wall interaction detected by the prolongation of the bleeding time. It can also result from a deficiency of clotting factors, detected by the prolongation of the prothrombin

time, the activated partial thromboplastin time, or both.

Efforts to minimize these adverse sequelae center on preoperative evaluation. Attempts should be made to identify patients at risk for hemorrhagic complications by history, physical examination and laboratory testing.¹² Though a positive history often indicates increased risk, a bleeding disorder may exist without being suspected until excessive surgical bleeding triggers evaluation of hemostasis.^{13, 14, 15}

On reviewing the literature, we came across no prospective reports which would demonstrate the relative merits of any or all of these screening procedures in predicting abnormal perioperative bleeding, and accordingly we designed the following study.

ABBREVIATIONS USED:

aPTT: activated partial thromboplastin time
CBC: complete blood count
ENT: ear, nose and throat
PT: prothrombin time
SBT: Simplate bleeding time
T&A: tonsillectomy and adenoidectomy

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Patients and Methods

Over a two-year period 250 consecutive patients between the ages of 1 and 19 years scheduled to undergo ENT procedures were enrolled in the study. Patients or their parents replied to questions designed to uncover a bleeding tendency. The questions asked were: Do you bruise easily; do you bleed heavily from wounds; do you have heavy menstrual periods; do you bleed frequently from the nose; have you required blood transfusions after surgery or dental extractions; does anyone in the family have a bleeding problem; are you currently taking any medications? A physical examination, a complete blood count (CBC) with differential, and the following hemostasis screening tests were performed routinely: a platelet count, the prothrombin time (PT) (normal range 9-13 seconds), and the activated partial thromboplastin time (aPTT) (normal range 24-37 seconds). Because of the discomfort and length of the procedure, the Simplate® bleeding time (SBT) (normal range 3-9 minutes) was not performed routinely. Rather, a history suggestive of a bleeding problem, a prolonged aPTT, or excessive perioperative bleeding were indications for measuring the bleeding time (82 subjects).

The CBC was done with a Coulter S Plus counter, and the differential and platelet counts were done manually. The aPTT and the PT were carried out according to manufacturer's instructions. For the bleeding time, a blood pressure cuff was inflated to 40 mm Hg, and a transverse incision six mm in length and one mm deep was made using the Simplate 1 device (General Diagnostics). The time required to stop bleeding was estimated to the nearest half minute.

Surgery was performed in the ambulatory surgical area by one

of two otolaryngologists. Acetaminophen was administered postoperatively for pain. Tonsillectomies were performed by dissection, using a snare and cautery as needed. An adenotome and curettes were used for the removal of adenoids. Myringotomies were mostly carried out on the anterosuperior aspect of the tympanic membrane, and Teflon® tubes were inserted.

Patients were observed for several hours following surgery for signs of hemorrhage or other complications. If none were present, they were discharged later in the day.

For the purposes of this study, excessive postoperative bleeding existed if the surgeon listed it specifically as a complication in the medical record, or if the patient required a transfusion, surgical hemostasis, an emergency room visit, or readmission due to hemorrhage.

Statistical analysis was performed using analysis of variance, chi square and correlation testing. The Student t test was used to obtain the appropriate P values.

Results

Of the 250 patients in the study, 123 were female and 127 were male. Their ages ranged from 1 to 19 years, with an average age of 5.9 ± 3.9 years. Sixty-one (24.4 percent) patients were below 4 years of age, 139 (55.6 percent) were between 4 and 8 years old, and 50 (20 percent) were 8 to 19 years old.

Eight patients (3.2 percent) bled excessively during or after surgery. Seven bled from the tonsillar bed; one bled from the ear following a myringotomy. In two patients bleeding occurred within 24 hours of surgery; in the other six it took place two to 14 days later.

Risk Factors by Preoperative History

In 75 cases (30 percent) there were positive responses; in 57 only one, in the remainder up to three. Surprisingly, in only one case — a boy with a family history of bleeding (case 3) — was a positive item predictive of abnormal bleeding. Case 1, who had no risk factors by preoperative history, took aspirin two days before bleeding on day 14. With the exception of case 3, none of the remaining 74 patients giving a positive preoperative history bled excessively. Only two of this group had an isolated, abnormal preoperative laboratory test: a 6-year-old girl with an SBT of 14 minutes bruised readily; another 10-year-old girl with an aPTT of 38.5 seconds had taken an antihistamine prior to surgery.

Hemostasis Screening Tests

The platelet count and prothrombin time were within the normal range in all patients, and the differences between those who bled and those who did not were not statistically significant.

In contrast, the mean aPTT of those who bled excessively was 37.5 ± 4.5 seconds as compared with 33.4 ± 3.4 seconds in those who did not ($p < 0.01$). The aPTT was greater than 37 seconds (two standard deviations above the mean) in 36 patients. Four of these patients (11 percent) bled, one during surgery, the other within the following 14 days. One was a young woman whose preoperative evaluation revealed type I von Willebrand's disease (case 6). She received cryoprecipitate preoperatively, followed by ten days of epsilon-aminocaproic acid orally, but hemorrhaged on the 14th day after eating potato chips. A 6-year-old boy whose aPTT was 40.7 seconds had factor XI deficiency. The other two had no definable disease.

The SBT was prolonged (greater than 9 minutes) in 8 of 92 patients (8.6 percent) in whom it was per-

The platelet count and prothrombin time were within the normal range in all patients, and the differences between those who bled and those who did not were not statistically significant.

formed. Three of these eight patients bled excessively, one during surgery, and two on the second and 14th postoperative day, respectively. Two of the three required transfusion. The mean Simplate bleeding time in postoperative bleeders was 7.3 ± 2.7 minutes, in contrast to 4.4 ± 2.8 minutes in the others ($p < 0.01$).

Discussion

Mild bleeding defects are recognized with increasing frequency as methods for studying hemostasis have become more sensitive and widespread.^{15, 18} Because they are not oblivious under the conditions of everyday living, their presence is more likely to be detected following surgical procedures such as the foregoing or after severe trauma. It is not surprising that the tonsillectomy is often said to be the ultimate test of hemostasis, perhaps because the tissues surrounding the removed tonsil or adenoid cannot collapse, nor is surgical hemostasis easily achieved. Accordingly, Fuller¹⁶ found that, of an estimated 195,000 surgical procedures in a referral metropolitan hospital over a 15-year period, 14 of 17 cases associated with a problem of hemostasis were T&As. Ten of the 17 had no personal or family history of a bleeding tendency, and in six, the screening tests were normal.

In undertaking this study we postulated that at least some patients bleeding excessively after otolaryngology procedures may have an underlying mild hemostasis problem. We were able to establish a definite one in two of our eight postoperative bleeders (cases 2 and 6). In cases 3 and 7 we suspected, but were unable to prove by more specific assays, von Willebrand's disease. Medications known to affect platelet function may have been contributory in cases 1 and 7. The child with mild factor XI deficiency would probably not have been detected were it not for his tonsillectomy. In four children, (cases 1, 4, 5, and 8) no definable disorder of hemostasis was found, although in case 1 the borderline bleeding time was suggestive of a functional platelet problem.

Of note is that a suggestive questionnaire was often not predictive of perioperative bleeding. This may be because minor bleeding disorders produce such subtle clinical signs and symptoms that they go unheeded. A person who has always bruised easily may perceive it as normal. Alternatively, our questions, asked in a busy office setting, may have been best answered in a less distracting environment.

Our data do show, on the other hand, that abnormalities of two of the laboratory tests, the aPTT and SBT, indicate a greater risk, notwithstanding our inability to establish a specific diagnosis in some. This is consistent with Bachmann's report¹⁵ in which an attributable cause of bleeding could not be found in 20 of 95 patients with mild bleeding disorders. Of note, six of these 20 had prolonged aPTTs, as in two of our patients (cases 3 and 7).

We confirm that hemorrhage remains today, as in the past, an appreciable postoperative complication following common ENT

procedures. A negative personal or family history, though reassuring, does not ease this concern, nor do abnormal screening tests always predict abnormal bleeding, though they indicate increased risk. Rather, one must combine an accurate history with preoperative screening tests, as well as warn about drugs known to increase bleeding risk. Once aware of an abnormal test, the clinician can do much to avoid a physically and emotionally traumatic experience. Prudence dictates that such patients be watched closely, preferably where means are available to arrest bleeding. When a diagnosis is established, preoperative management with specific drugs or plasma products significantly decreases the risk of surgery. In less defined disorders, correction of the tests and adequate hemostasis were achieved using prednisone¹⁸ or desmopressin acetate.¹⁹

... we must emphasize that half of our cases bled excessively despite unremarkable history and tests, which suggests that the tonsillectomy in the absence of other risk factors is not innocuous.

Finally, we must emphasize that half of our cases bled excessively despite unremarkable history and tests, which suggests that the tonsillectomy in the absence of other risk factors is not innocuous. Performing such common surgery only when there is no doubt about the benefit remains good advice, even as the sensitivity of our tests has increased our vigilance.

Table 1 Profile of Patients Who Bled Excessively Within Postoperative Period

Patients	Age	Sex	Hist.	Meds.	Plts.	PT	aPTT	SBT	Op.	Bleeding	Comments
1) E.A.	6	F	(-)	(-)	260	100%	35.5	9	T,M	14 days postop	Took ASA postoperatively
2) S.A.	14	M	(-)	(-)	236	83%	40.7	7	T	10 days postop	Factor XI deficiency = 37%
3) D.A.	3	M	(+) ¹	(-)	254	100%	38.6	10	T	Intraop	No definable abnormality
4) M.C.	3	M	(-)	(-)	297	100%	34.1	5	T	Intraop	No definable abnormality
5) E.D.	6	F	(-)	(-)	358	100%	35.9	6	T	6 days postop	No definable abnormality
6) R.H.	19	F	(-)	(+) ²	308	98%	42.5	8	T	11 days postop	von Willebrand's disease
7) A.M.	6	F	(-)	(+) ³	332	97%	43.8	11	M	2 days postop	No definable abnormality
8) A.S.	5	F	(-)	(-)	385	100%	29.3	2	T	5 days postop	No definable abnormality

Key: Hist. — History preoperatively: questions 1-6.

Meds. — Medications being taken prior to surgery.

Op. — Type of operation performed (T — tonsillectomy or tonsillectomy plus adenoidectomy; M — bilateral myringotomy; T,M — tonsillectomy with or without adenoidectomy plus myringotomy).

1 — Positive answer to question 6 — family history of bleeding problems.

2 — Patient was on tetracycline prior to surgery.

3 — Patient was on PCN and antihistamine decongestant prior to surgery.

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References

- Bluestone CD: Workshop on tonsillectomy and adenoidectomy. *Ann Oto Rhinol Laryngol* 1975;(suppl 19):84:1-76.
- Nathan MD, Sessions DG: Massive posttonsillectomy hemorrhage. *South Med J* 1981;74:1153-1156.
- Fox SL: Bleeding following tonsillectomy. *Laryngoscope* 1952;62:414-425.
- Carmody D, Vamadevan T, Cooper SM: Post tonsillectomy haemorrhage. *J Laryngol Otol* 1982;96:635-638.
- Crysdale WS, Russel D: Complications of tonsillectomy and adenoidectomy in 9409 children observed overnight. *Can Med Assoc J* 1986;135:1139-1142.
- McKenzie, W, Comb MB: The risks of tonsillectomy. *Lancet* 1953;2:958-960.
- Pratt LW: Tonsillectomy and adenoidectomy: mortality and morbidity. *Trans Am Acad Ophthalmol Otolaryngol* 1970;74:1146-1152.
- Proctor DF, Douglass CC: Bleeding following tonsil and adenoid operations. *Trans Am Acad Ophthalmol Otolaryngol* 1958;62:592-597.
- Chowdhury K, Tewfik TL, Schloss MD: Post-tonsillectomy and adenoidectomy hemorrhage. *J Otolaryngol* 1988;17:46-49.
- Cummings GO: Mortalities and morbidities following 20,000 tonsil and adenoidectomies. *Laryngoscope* 1954;64:647-655.
- Williams JD, Pope TH Jr: Prevention of primary tonsillectomy bleeding. *Arch Otolaryngol* 1973;98:306-309.
- Tami TA, Parker GS, Taylor RE: Post-tonsillectomy bleeding: an evaluation of risk factors. *Laryngoscope* 1987;97(11):1307-1311.
- Rapaport SI: Preoperative hemostatic evaluation: Which tests, if any? *Blood* 1983; 61:2299-231.
- Watson-Williams EJ: Hematologic and hemostatic considerations before surgery. *Med Clin of North Am* 1979;63:1165-1189.
- Bachmann F: Diagnostic approach to mild bleeding disorders. *Semin Hematol* 1980;17:292-305.
- Fuller AM: Evaluation and management of coagulation disorders in elective surgical patients. *Laryngoscope* 1981;91:1484-1500.
- Kiley V, Stuart JJ, Johnson CA: Coagulation studies in children with isolated recurrent epistaxis. *J Pediatr* 1982;100:579-581.
- Mielke CH, Levine PH, Zucker S: Preoperative prednisone therapy in platelet function disorders. *Thromb Res* 1981;21:655-662.
- Kobrinsky NL, Gerrard JM, Watson CM et al: Shortening of bleeding time by 1-deamino-8-arginine vasopressin in various bleeding disorders. *Lancet* 1984;1145-1148.

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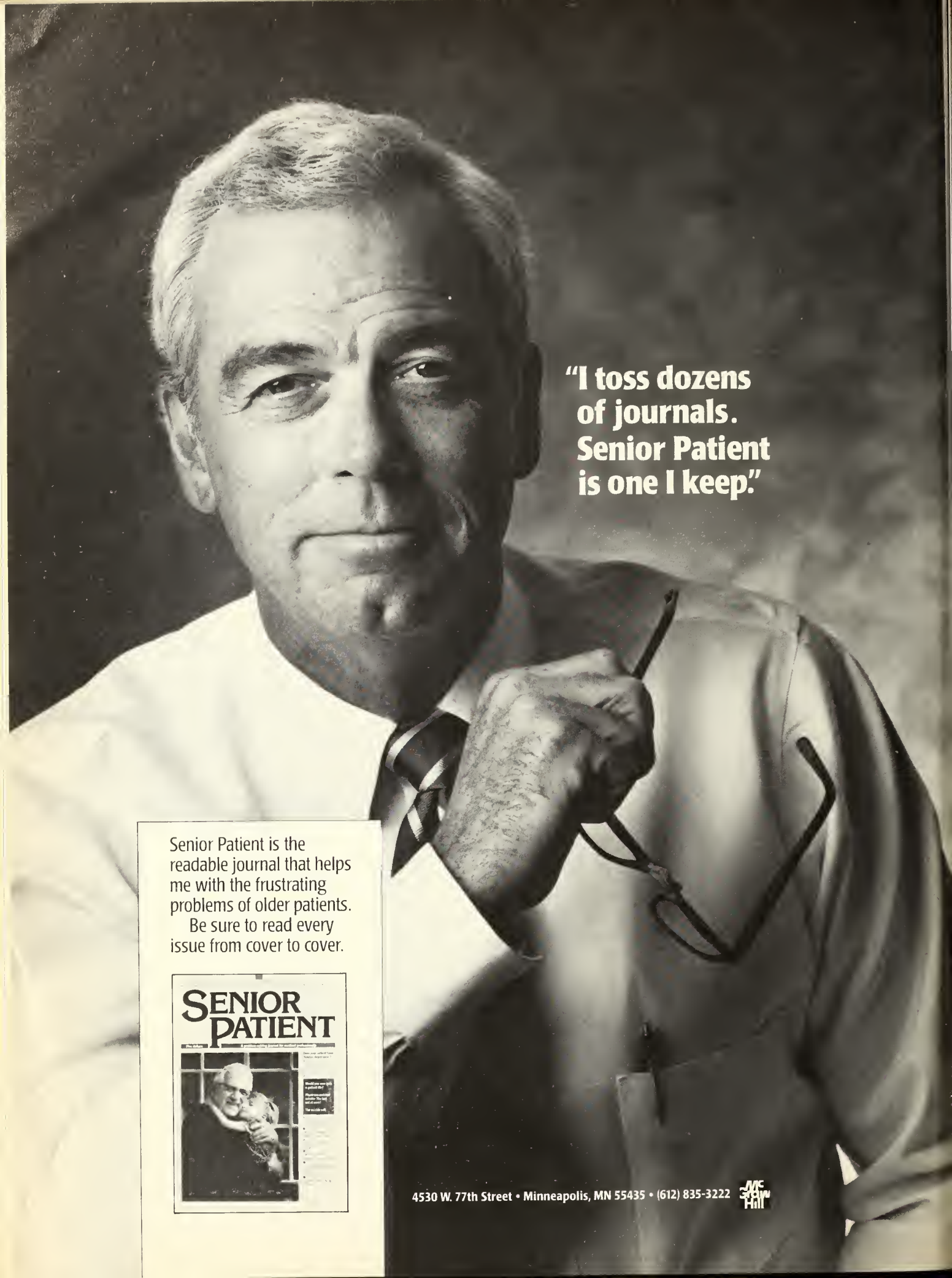
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Superior Vena Cava Syndrome

Michelle Segall
Stephen A. Shore, MD
Marilyn E. Miller, MD

... the most likely factors contributing to the thrombosis was the indwelling venous catheter together with an underlying hypercoagulable state attributable to a malignancy.

Obstruction of the superior vena cava (SVC) results when this thin-walled vessel is invaded, compressed, and/or thrombosed.¹ Blockage of blood flow leads to the Superior Vena Cava Syndrome (SVCS) with typical symptoms of suffusion, dyspnea, cough, and less commonly pain, syncope, dysphagia, and hemoptysis. The most important physical findings are the collateral ve-

nous pattern covering the anterior chest wall and the dilated neck veins with edema of the face, arm, and chest.²

We present a case of SVCS secondary to central venous catheter thrombosis in a patient with metastatic breast cancer on hormonal therapy. Pathophysiology, treatment, and prognosis are discussed.

Case Report

A 64-year-old female presented with facial swelling, shortness of breath, orthopnea, anorexia, weakness, and malaise. On physical examination, she had a distended collateral venous pattern over the anterior thorax and neck with facial swelling and edema of the right arm. A diagnosis of stage IV breast cancer had been made in June, 1986, when she presented with an ovarian mass, ascites, and a breast mass. The ovarian and breast masses were identical histologically.

Systemic chemotherapy with Cytoxan®, methotrexate, 5-fluorouracil, and tamoxifen were instituted in July, 1986. Her course was complicated by a left pleural effusion, bacterial peritonitis and abdominal wall cellulitis with as-

sociated lower extremity deep vein thrombosis. These complications occurred between July and September, 1986. She was treated with intravenous heparin followed by oral Coumadin® for one year. In November, 1986, a subcutaneous Infus-A-Port® was inserted into the right subclavian vein. Combination chemotherapy was completed in March, 1987, and she was maintained on tamoxifen thereafter. A right clavicular pathologic fracture was diagnosed in May, 1988, and at that time, a bone scan showed multiple metastatic lesions. Radiation therapy to the right clavicle was initiated, and tamoxifen was discontinued. In August, 1988, Megace® was instituted when a bone scan showed additional areas of metastatic disease. Her carcinoembryonic antigen level increased to 21 (normal up to 5) in April, 1989.

Positive findings on physical examination were compatible

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ABBREVIATIONS USED:

CMF: cytoxan-methotrexate-5FU

SVC: superior vena cava

SVCS: superior vena cava syndrome

with superior vena cava syndrome. There was orthopnea and the respiratory rate was 28, with audible wheezing. Blood pressure was 120/80 without evidence of pulsus paradoxus. Pulse was 90. Face was edematous. The jugular veins were distended. The anterior chest wall showed a dilated venous pattern. The right upper extremity was larger than the left. Diffuse expiratory wheezes were heard throughout both lung fields. Cardiac exam was normal, and there was no evidence of hepatosplenomegaly.

Pertinent laboratory data was compatible with superior vena cava syndrome. Chest x-ray was within normal limits; specifically, there was no evidence of a mediastinal mass. Injection of contrast through the Infus-A-Port® demonstrated complete obstruction of the superior vena cava at the level of the right atrium with significant collateral blood flow. A ventilation perfusion lung scan was highly suspicious for pulmonary embolus. Streptokinase was infused through the port. A loading dose of 250,000 units was administered followed by continuous infusion of 100,000 units. Re-examination of the superior vena cava in 24 hours was compatible with complete resolution of the thrombus. There was also dramatic clinical improvement noted at the same time.

Discussion

The etiology of superior vena cava syndrome has changed dramatically in the past few years because of the widespread use of indwelling venous catheters.¹ Numerous reports have appeared linking central venous catheters, transvenous pacemakers and central hyperalimentation lines to thrombosis of the superior vena cava. In a review of this syndrome from 1961-1981 at the Mayo Clinic, SVC was caused by malignant

neoplasms in 78 percent of 86 patients.² Of this number, 45 cases were attributed to lung neoplasms. Breast carcinoma and lymphoma accounted for seven and eight cases respectively. In a literature review conducted at the University of Arizona,¹ small cell carcinoma and squamous cell carcinoma of the lung were identified as the most common causes of the syndrome representing 47 percent of 1,986 cases. Other nonmalignant causes were infrequent and included mediastinal fibrosis, inflammatory enlarged lymph nodes and radiation fibrosis.

Numerous reports have appeared linking central venous catheters, transvenous pacemakers and central hyperalimentation lines to thrombosis of the superior vena cava.

The exact complication rate of thrombosis due to indwelling central venous catheters is unknown. Symptomatic subclavian vein thrombosis occurs in 2-10 percent of patients requiring prolonged central venous catheterizations.^{4, 6} Clinically asymptomatic subclavian vein thrombosis detected only by angiography or radionuclide studies has been reported in 20-70 percent of patients with subclavian catheters.^{4, 6} Subcutaneous implanted venous access systems composed of a reservoir and silastic catheter have been associated with venous thrombosis. The major complication of these systems has reportedly been subclavian or jugular venous thrombosis occurring in 15 out of 92 patients studied (16 percent). In all reported cases, the subclavian vein obstruction was total, and in 14/15 it was confirmed by venography. In none of these 15 patients

was the superior vena cava thrombosed.⁴ Once the diagnosis of the SVCS has been established, it is essential to make a pathologic diagnosis. Several concerns were expressed in the past about the safety of establishing a pathologic diagnosis. Included among these were, that diagnostic procedures had a significant risk of bleeding. The available data does not support this concern.¹ Ahmann reported that out of 197 contrast venograms performed, there was only one patient with transient respiratory distress reported. Therefore, only minimal evidence suggests that diagnostic procedures carry an increased risk in patients with SVCS. The establishment of a pathologic diagnosis is of considerable importance as malignancies may account for the greatest number of SVCS. The most productive investigations in establishing the diagnosis are lung biopsy, bronchoscopy, and biopsy of superficial lymph nodes.

The mortality reported with SVCS is minimal.¹ In actuality, a review of almost 2,000 cases clearly showed that there was only one death directly related to superior vena cava obstruction, and in that case, the death occurred because of aspiration.¹ The life-threatening nature of the SVCS is noted when the trachea is obstructed by a superior mediastinal mass. Otherwise, complications are exceedingly rare and are not necessarily correlated with the obstruction of the vessel. These include syncope, seizures, cerebral edema, and stridor secondary to laryngeal or glossal edema. As thrombosis accounts for an increasing number of cases, pulmonary embolism has become an additional complication. Survival, however, is correlated with the underlying cause of the syndrome and not because of the presence or absence of superior vena cava syndrome or to

the success in relieving the obstruction. In cases with malignant etiology, survival was closely correlated with the prognosis of the underlying tumor type. Therefore, although it is not a medical emergency, there exists the potential for developing complications. The primary goal in diagnosis and treatment is to decrease morbidity and circumvent further complications.

Therapy of the syndrome is directly related to its etiology. In those instances of malignant obstruction, the standard treatment has included radiation therapy, chemotherapy, and corticosteroids. Approximately 50-70 percent of treated patients are symptomatically improved within two weeks.¹ When thrombosis is the cause of the SVCS, fibrinolytic therapy has emerged as an effective means of relieving obstruction.⁵ There are no prospective studies on the various type of fibrinolytic therapy; however, it has been reported that venous thrombosis due to a transvenous pacemaker rapidly responded to streptokinase infusion with objective regression of the obstruction.⁵ Urokinase has been used in several cancer patients with axillary and subclavian venous thromboses due to percutaneous central venous catheters. Urokinase was found to be highly successful when locally infused into the thrombus.^{4,6,9} In one study, lower doses of locally infused fibrinolytic agents were used rather than systemic doses. Twenty-five out of thirty thrombi were lysed when directly infused in this way.⁶ Tissue plasminogen activator is another agent which has been used in SVCS secondary to thrombosis of the Hickman catheter.⁷ One obvious question which arises in the management of these patients is whether or not the central catheter should be removed. Many patients with malignant disease will

require further chemotherapy. However, in those with incomplete recanalization or with residual thrombosis in whom central venous lines are not removed there is an increased risk of developing a second thrombosis.⁶

In our patient, superior vena caval thrombosis was objectively documented, and infusional streptokinase therapy resulted in complete vessel patency within 24 hours. The likely mechanism leading to thrombus formation could have been related to several factors including a previous history of thrombosis. Also important is the association of thrombosis with malignancy. The incidence of such events in patients with malignant disease is 5-15 percent.^{8,10} Several basic mechanisms involved in the activation of the blood coagulation system have been described in patients with neoplasms. Included among these are platelet activation by tumor cells; production of procoagulants; cells stimulated by tumor antigens, as well as the direct production of procoagulants by tumor cells.⁸ Chemotherapy has also been associated with an increased incidence of thrombosis by several potential mechanisms. Sclerosing agents may disrupt normal endothelium and ultimately lead to thrombosis. In one study, 42 percent of patients developed subclavian thrombosis while receiving chemotherapy.⁹ Chemotherapy, especially in breast cancer patients, has been associated with endogenous anticoagulant perturbation. In a recent study, serial coagulation studies on 15 women during cytoxan-methotrexate-5FU (CMF) therapy showed decreased levels of protein C, a major vitamin K dependent inhibitor of blood coagulation and a profibrinolytic agent.¹⁰ There also were decreases in levels of protein S a cofactor for pro-

tein C. Decreases in both these levels are associated with increased risks of thromboembolic disease. However, none of the women in this study developed a clinically evident thromboembolic event. Tamoxifen has been shown to have paradoxical estrogenic effects as shown by lowered levels of antithrombin III.¹¹ The reported patient had been off tamoxifen therapy for more than one year, and, therefore, it is difficult to attribute this event to ingestion of tamoxifen. However, when the thrombus developed, she was on a progestational agent, Megace.[®] There have been no reported studies implicating Megace[®] with hypercoagulability or with predisposition to thrombosis. Studies comparing the effects of estradiol, progesterone, and cortisol on the synthesis and catabolism of antithrombin III showed that progesterone had no appreciable effect on antithrombin III metabolism.¹²

Clinically asymptomatic subclavian thrombosis detected only by angiography or radionuclide studies has been reported in 20-70 percent of patients with subclavian catheters.

In the present patient, the most likely factors contributing to the thrombosis was the indwelling venous catheter together with an underlying hypercoagulable state attributable to a malignancy. Further studies need to be conducted comparing the incidence of thromboses of venous access lines and also in elucidating whether or not patients ingesting Megace[®] do have an increased incidence of thrombotic events. Fortunately, in our case, the diagnosis was made quickly and the thrombus was rapidly lysed with streptokinase.

References

- ¹ Ahmann FR: A reassessment of the clinical implications of the superior vena caval syndrome. *J Clin Onc* 2:961-969, 1986.
- ² Parish SM, Marschke RF, Dines DE, et al: Etiologic considerations in superior vena cava syndrome. *Mayo Clinic Proc* 56:407-413, 1981.
- ³ Torosian MH, Meranze S, McLean G, Mullen JL: Central venous access with occlusive superior central venous thrombosis. *Ann Surg* 203:30-33, 1985.
- ⁴ Lokich JJ, Bothe A, Benotti P, Moore C: Complications and management of implanted venous access catheters. *J Clin Onc* 3:710-717, 1985.
- ⁵ Katz PO, Hachshaw BT, Barish CF, Powell BL: Venous thrombosis as a cause of superior vena cava syndrome. *Arch Int Med* 143:1050-1052, 1983.
- ⁶ Fraschini G, et al: Local infusion of urokinase for the lysis of thrombosis associated with permanent central venous catheters in cancer patients. *J Clin Onc* 5:672-678, 1987.
- ⁷ Fine D, Shepherd RFJ, Welch T: Thrombolytic therapy for superior vena cava syndrome. *Lancet* 1200-1201, 1989.
- ⁸ Schafer, AI: The hypercoagulable states. *Ann Int Med* 102:814-828, 1985.
- ⁹ Lokich JJ, Becker B: Subclavian vein thrombosis in patients treated with infusion chemotherapy for advanced malignancy. *Cancer* 52:1586-1589, 1983.
- ¹⁰ Rogers JS, Murgo AJ, Fontana JA, Raich PC: Chemotherapy for breast cancer decreases plasma protein C and protein S. *J Clin Onc* 6:276-281, 1988.
- ¹¹ Enck RE, Rios CN: Tamoxifen treatment of metastatic breast cancer and antithrombin III levels. *Cancer* 53:2607-2609, 1984.
- ¹² Kobayashi N, Takeda Y: Studies of the ef-

fects of estradiol, progesterone, cortisol, thrombophlebitis, and typhoid vaccine on synthesis and catabolism of antithrombin III in the dog. *Thrombos Haemostas* 37:11-121, 1977.

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Solitary Cervical Node Metastasis in Renal Cell Carcinoma

George N. Tzanakakis, MD
Kilmer S. McCully, MD
Michael P. Vezeridis, MD

This patient . . . is alive without evidence of disease three years following treatment.

Adenocarcinoma of the kidney is known for its tendency to metastasize widely as well as to unusual locations. One of the unique features of this tumor is its propensity to metastasize to the head and neck region and most commonly to the nasal cavity, paranasal sinuses, skin, larynx, jaw, temporal bones, parotid and thyroid glands.^{1, 2, 3} However, isolated metastases to cervical lymph nodes are uncommon.^{4, 5, 6} We are

reporting herein a case of hypernephroma with a solitary metastasis to a cervical lymph node which was the only initial sign at presentation; this led to the diagnosis and resection of both the primary tumor and the metastasis and resulting in long-term survival.

Case Report

A 66-year-old white male was admitted to the Providence Veterans Administration Medical Center with an enlarged lymph node on the left side of the neck which was discovered during a routine physical examination. His past medical history was remarkable for hypertension controlled with Moduretic,[®] non-insulin dependent diabetes controlled with diet, remote appendectomy and alcohol abuse. Physical examination revealed a 3.5 × 4.5 cm hard, non-tender left cervical mass. There were no other enlarged nodes present and the rest of the physical examination was unremarkable. Biopsy of the cervical mass showed poorly differentiated adenocarcinoma consistent with lung or kidney. Chest x-ray and tomograms showed no evidence of a lung primary. Computerized axial tomography (CT)

of the abdomen and pelvis showed multiple renal cysts and a mass in the left kidney which appeared to be hypovascular in an arteriogram. A CT-scan guided needle biopsy of the mass was positive for renal cell carcinoma. The patient underwent excision of the left neck mass. The entire mass was removed along with several enlarged lymph nodes. Histologic examination of the main mass again showed metastatic adenocarcinoma (Fig 1) while the other nodes were found to be free of tumor. Two weeks following the excision of the cervical metastasis the patient was taken again to the operating room where a left radical nephrectomy was performed. The left kidney had a large mass at the mid-portion which histologically was found to be clear cell adenocarcinoma with papillary pattern (Fig 2). There was no invasion of the capsule or veins. The postoperative course was unremarkable and he was discharged on the seventh postoperative day. He received a course of 4500 rad of radiation therapy to the left su-

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ABBREVIATIONS USED:
CT: computerized axial tomography

praclavicular fossa, which he tolerated well. He is alive and free of disease three years following the initial diagnosis.

Discussion

Approximately one third of patients with renal cell carcinoma have distant metastases at their initial presentation.⁷ Most common sites of metastases are the lung, bones, liver, and adrenals.⁵ Metastases have been observed as late as fifty years following nephrectomy.⁸

... it seems reasonable to advocate surgical removal if it can be accomplished with minimal morbidity. This approach is justified in view of the unpredictable behavior of this tumor and the lack of effective systemic treatment.

It is estimated that between 14 percent and 16 percent of patients have metastases above the clavicle and in approximately 8 percent the presenting clinical manifestation of this tumor is disease in the head and neck region.^{4,5} In this region metastases most commonly occur in the nasal cavity, paranasal sinuses, skin, larynx, jaws, temporal bones, parotid and thyroid.^{1,2,3} The explanation for the apparent propensity for metastases to this region remains somewhat unclear. The most reasonable explanation for this phenomenon appears to be tumor embolization via Batson's plexus of extensive anastomoses between the avascular vertebral and epidural venous systems.⁴ In this manner the vertebral venous plexus can bypass the pulmonary venous system producing metastases to the head and neck region without involving the lung.

Solitary metastasis to a cervical lymph node from renal cell car-

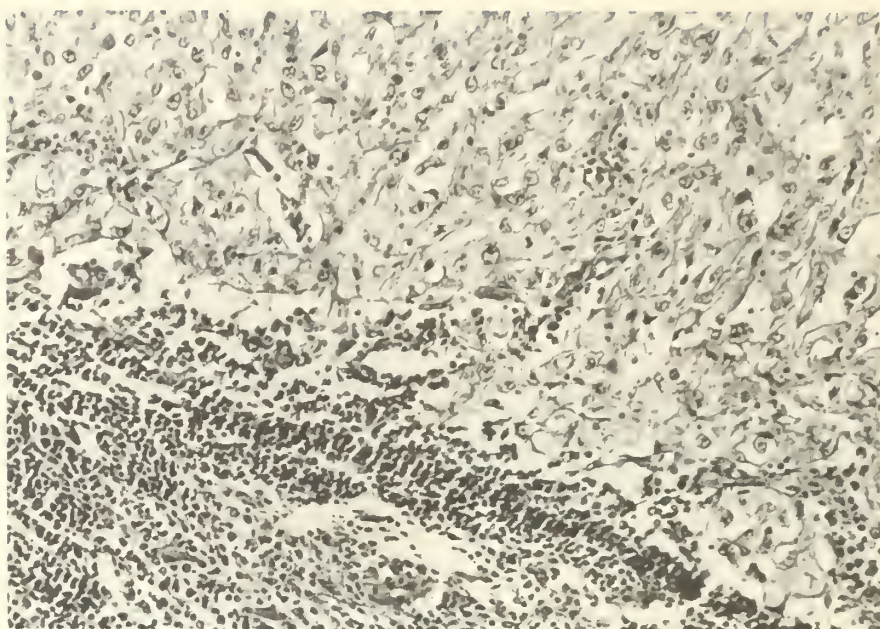


Figure 1. Lymph node containing metastatic clear cell carcinoma. H + E \times 188.

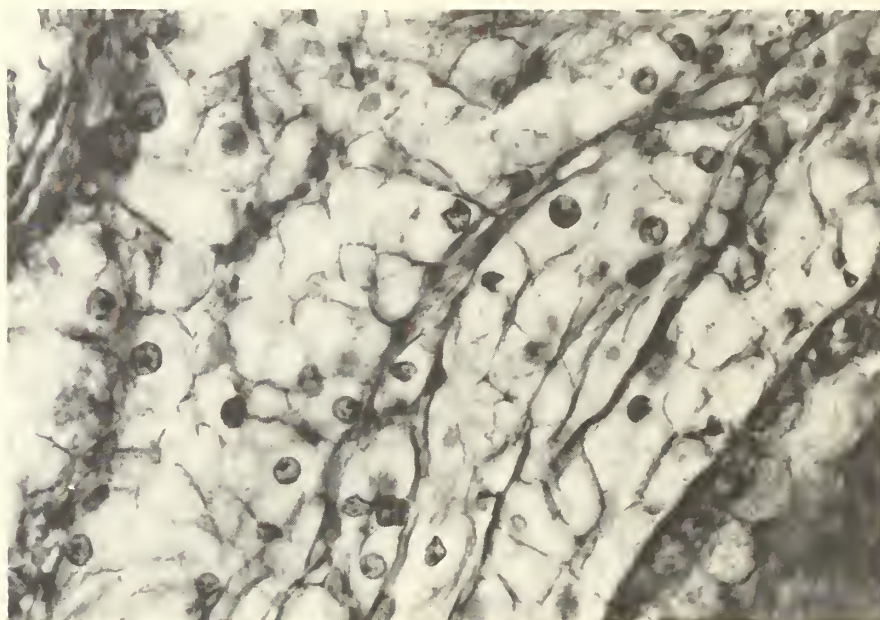


Figure 2. Photomicrograph of the primary renal carcinoma. Cells with clear cytoplasm and distinct plasma membranes are arranged in cords. H + E \times 450.

cinoma is a rather uncommon occurrence. Our search of the English literature revealed only four reported cases.^{4,5,6} In the case we are reporting the metastasis to the cervical node was actually the presenting finding which led to the diagnosis of renal cell car-

noma. The patient was otherwise asymptomatic and the involved node was found during a routine physical examination. The presence of supraclavicular metastases from renal cell carcinoma has generally been regarded as a sign of advanced disease.^{9,10} This

patient however is alive without evidence of disease three years following treatment. Although a definitive conclusion regarding the optimal management of isolated distant metastases to cervical node from renal cell carcinoma can not be drawn from the limited number of reported cases, it seems reasonable to advocate surgical removal if it can be accomplished with acceptable morbidity. This approach is justified in view of the unpredictable behavior of this tumor and the lack of effective systemic treatment.

References

¹ Batsakis, JG: Tumors of the head and neck: Clinical and pathological considerations, 2nd ed. Baltimore: Williams and Wilkins p. 240, 1979.

² Bernstein, JM, Montgomery WW, and Balogh, K Jr: Metastatic tumors to the maxilla, nose and paranasal sinuses. *Laryngoscope*, 76:621, 1986.

³ Nahum, AM, Bailey, BI: Malignant tumors metastatic to the paranasal sinuses: Case report and review of the literature. *Laryngoscope* 73:92, 1963.

⁴ Boles, R, Cerny, J: Head and neck metastases from renal carcinomas. *Mich Med*, 70:616, 1971.

⁵ Miyamoto, R, Helmus, C: hypernephroma metastatic to the head and neck. *Laryngoscope*, 83:898, 1973.

⁶ Som, PM, Norton, KI, Shugar, JM, Reede, DL, Norton, L, Biller, HF, and Som, ML: Metastatic hypernephroma to the head and neck. *A J N R*, 8:1103, 1987.

⁷ Holland, JM: Cancer of the kidney - natural history and staging. *Cancer*, 32:1030, 1973.

⁸ Walter, CW, Gillespie, DR: Metastatic hypernephroma of fifty years duration. *Minn Med*, 43:123, 1960.

⁹ Jakobson, E: Über die klinische bedeutung der Untersuchung der supraklavikulären lymphknoten bei krebs. *Acta Chir Scand*, 96:75, 1984.

¹⁰ Klingenberg, I: Histopathologic findings in the prescalene tissue from 1000 post-mortem cases. *Acta Chir Scand*, 127:57, 1964.

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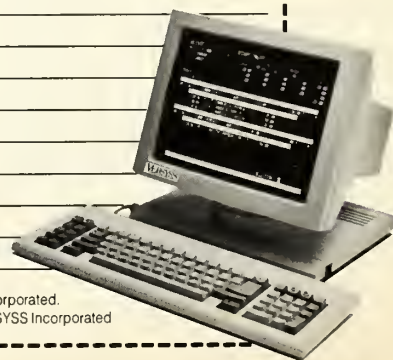
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Self-Enucleation: Pathology and Treatment

Hugo H. Halo, MD
Thomas A. Jordan, MSW, LICSW
Ronald Mark Stewart, MD
Susan E. Apshaga, MA

... and if thy right eye offend thee, pluck it out and throw it away; for it is profitable for thee that one of thy members should perish, and not that thy whole body should be cast in hell.¹⁹

The patient who has gouged out one or both eyes presents many difficult and pressing questions to mental health practitioners. The need to examine and understand the factors controlling this grave

event is immediate, as is the need to control this aggressive response known as self-enucleation.

The authors will not focus specifically on other forms of self-mutilation wherein a person damages an eye, cuts off a finger or hand, mutilates genitals, or cuts out the tongue. We will address issues concerning self-enucleation which other clinicians will need to know. The most immediate questions are: What should we do? How should we calm the patient? What risk does the patient pose to others? Why has this patient gouged out his/her eye(s)?

The case herein presented shares several important factors with other cases reviewed. At the time of enucleation, the patient was in a state of psychosis. She suffered religious delusions, real and or imagined guilt, and had a tyrannical conscience. The guilt was displaced to the right eye, and the successful completion of ocular removal was followed by relief of anxiety. J. P. Gerhard, in "A Propos des Automutilations Oculaires" reported that data on persons who had self-enucleated showed diagnoses of *delire mystique*, hallucination, psychosis, *periodique melancholic delirante*, *melancholic schizophrenia*,

post encephalitis, and LSD psychoses.¹

In an article titled "Rescuing the Angel Within" Muscovitz and Byrd associated self-enucleation with acute phencyclidine intoxication.² The subject of our study was, for religious reasons, opposed to the use of drugs and she sometimes resisted prescribed medications. In this case, the guilt was real and confirmed by a Superior Court judge who sentenced the patient to a lengthy prison term for murdering her infant son by repeated stabbings. An indication of the patient's acceptance of the guilt is her refusal to plead not guilty by reason of insanity. Her rejection of her psychiatric illness placed the blame solely upon herself in terms of her own philosophy and understanding.

Much is learned about the mentally ill through the evaluations and assessments of mental health professionals who often work together. Psychiatrists, psychologists and social workers function as teams in a forensic setting. Together they possess the knowledge, skills, and criteria necessary to describe defendants' mental conditions, patho-

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logical beliefs and motivations, and to explain with particular regard to mental capacity and the crime charged how these factors influenced or could have influenced the defendant's behavior.³

Once the clinical assessments are completed, the psychosocial history or psychiatric profile of the patient (defendant) should also be complete, but not to the extent that assessments are not ongoing as changes occur in the patient, the situation and or circumstances. The subject of this study went through the cycle of being a patient, defendant, convicted felon, and eventually, convicted patient.

Review of the Literature

Self-enucleation, also known as self-ocular removal and Oedipism, is rare among the psychiatric population. Also rare is self-inflicted blindness.

The term, Oedipism, is derived from the mythical character in Sophocles' *Oedipus Rex*. Oedipus, in fulfillment of an oracle, kills his father and marries his mother. When confronted with the realities of his situation, Oedipus gouges out both of his eyes.⁴

In a publication entitled "Gods and Myths of Northern Europe," Ellis Davidson writes of Odin, a Norseman who gave his right eye for the right to drink a single draught from the spring of Mimir, waters which contained wisdom and understanding.⁵ In "Auto-enucleation of the Eye: A Study of Self-Mutilation," S. I. Davidson recounted an episode from 13th Century Baghdad.⁶ Marco Polo, upon reaching the City, reportedly was told of a cobbler possessed by sinful thoughts when the leg of a woman was exposed to him as he fitted her slippers. Overwhelmed with guilt, the cobbler destroyed his right eye with an awl.

Both women and men are represented among the medical studies of self-enucleation, with men representing the majority. Those who have self-enucleated one or both eyes include Jews, Protestants, Catholics and other religions. The races and nationalities vary. The ages range from 18 to 56. There are reports of auto-mutilation to the cornea by two children as young as 8 and 12 years old in the Netherlands.⁷ Tools used to enucleate have included fingers, razor blades, plastic forks, indeed, anything available at the time.

Self-enucleation, also known as self-ocular removal and Oedipism, is rare among the psychiatric population.

In 1976, McLean and Robertson reviewed the literature on self-enucleation covering the period 1846 to 1968.⁸ They reviewed 13 cases and added two of their own. In 1979, Tapper, Phil, Blond and Danyluk presented a single case study of self-inflicted blindness.⁹ In their search for older and less accessible literature covering the period from 1846 to 1961, they reviewed data including 15 cases of unilateral enucleation, seven cases of bilateral enucleation, and two cases of self-inflicted blindness.

In 1981 Yang and associates reported two cases of self-inflicted mutilation of the eyes, with one ending with self-enucleation of the left eye.¹⁰ Shore and associates reported one case in which a man enucleated both his eyes and another in which a patient stuck a pencil through the inner canthus of his right eye.¹¹

Feldshuh, Zasloff and Frosch reported a case of bilateral enucleation in 1977 in a paper entitled: "If thy right eye offend thee."¹²

Muscovitz and Byrd reported two cases of self-enucleation in 1983,¹³ Westermeyer reported one case in 1972,¹⁴ and Rosen and Hoffman reported two cases in 1972.¹⁵ Prior to our own article, the last two cases of self-enucleation were reported by Gail Eisenhower in 1985.¹⁶

For this article, foreign as well as American periodicals were reviewed and the search extended well beyond the usual computerized search which, in periods earlier than 1960, is limited. It is interesting to note that in a publication in India, S. W. Cooper reported two cases in: "Self-Inflicted Ocular Injuries."¹⁷ In these cases it was suspected that the motives were financial. Reportedly, there was an absence of suffering from any obvious mental illness. Dr Cooper expressed the opinion that a man will go to considerable lengths to get one eye blinded for the sake of a thousand rupees. He focused on ways in which insurance companies might protect themselves from persons who self-inflict eye injuries for the purpose of collecting compensation. In this particular article, mental illness was not an issue.

Perhaps the most beneficial results of research of this kind are the understanding and awareness of the contradictory picture preceding self-enucleation and other forms of violence among the psychiatric population. In general, patients who are incorrectly oriented and who have impaired concentration, poor memory and comprehension, are prone to become violent when provoked or intimidated. Violence and dangerousness cannot be predicted with reasonable accuracy.¹⁸

Common factors among the cases reviewed in the psychiatric literature, as well as our own study, included instances of distorted reality and an attempt to

use biblical references to support the distortion. The verse from Matthew 5:29 appeared most frequently: "and if thy right eye offend thee pluck it out and throw it away; for it is profitable for thee that one of thy members should perish, and not that thy whole body should be cast into hell."¹⁹

There are patients who constantly dwell on their religious beliefs and use them as reinforcements against guilt. Our subject confessed at one time that she was prompted by God and the devil to kill her baby son. On one occasion she compared the act to the deadly thought of Abraham towards his son, Isaac, but an angel intervened. The patient subsequently blamed herself rather than God or the devil, or her psychiatric illness for the death of her child. She enucleated her right eye.

The Case of Alice Adams

Alice Adams, not the subject's real name, was admitted to the psychiatric ward after plucking out her right eye. At the time, she had been sentenced to twenty years in the women's prison for the stabbing death of her nine-month-old son. Alice at this time was thirty-nine years old.

Initially, Alice had declared that she'd been prompted by "God or the Devil" to stab her son and pleaded innocent by reason of insanity, but then changed her mind and pleaded guilty to second degree murder.

The prison sentence of twenty years did not satisfy Alice's determination to be made accountable for her son's death. Subsequently, she attempted suicide in prison. This was later followed by the plucking out of the right eye.

A review of Alice's early history disclosed that as a child she was frequently moody and subject to temper tantrums. The moodiness continued throughout adoles-

cence. Alice was also a loner, but this did not hamper her academic endeavors throughout high school. The relationship between Alice, her parents, younger brother and sister reportedly was positive. During her college years, Alice became more sociable. She engaged in social drinking of alcoholic beverages and even experimented with marijuana.

The deaths of Alice's mother and father in 1971 and 1972 respectively were followed by periods of religious preoccupation and delusions. During the period between 1972 and 1985, there were several hospital admissions and discharges due primarily to overwhelming anxiety and obsessive symptomatology. A variety of psychiatric disorders had been applied to Mrs Adams during that period.

The 1980s began with Alice maintaining considerable stability. She worked in a book store, married and parented two children. Subsequent to her admission to the psychiatric hospital, Alice never discussed what caused the breakup of her marriage, other than to blame it on financial difficulty.

The divorce was planned according to Alice and by mutual consent. Mr Adams would retain custody of their two-and-one-half-year-old daughter and Alice would retain custody of their nine-month-old son. Shortly after Mr Adams and the daughter vacated the home, on a day at home alone with her son, Alice stabbed him eight times. She then telephoned police and awaited their arrival and arrest.

Psychiatric Hospitalization

Immediately after the self-inflicted ocular removal, Alice was rushed to a local hospital. After treatment there was a medical follow-up to protect the left eye. Initially Alice was reportedly re-

lieved and felt she had satisfied her need for punishment. She then was admitted to a state psychiatric hospital ward on an emergency certificate. Although a patient, she was a convicted felon and her status remained as such.

During the admission process, Alice exhibited immediate symptoms requiring the attention of the clinical staff. These symptoms included religiosity, self blame, and thoughts of reference from other people's thoughts. The affect displayed by Alice was flat and her energy level was characterized as low. Early on she was not significantly depressed or suicidal. Only gradually did she become extremely frustrated, obsessive, and pre-occupied.

During the initial stages of assessment and treatment, Alice became more unrealistic. Occasionally she would state that she "did not have a mental illness" and that she had "no psychotic disturbance." The preoccupation with wanting to return to the women's prison was ongoing. Alice would repeat to the staff, "I cannot stand it here! I cannot stand it here!" These vocal denials of her illness were sometimes accompanied by equally unrealistic expectations with regard to a reconciliation with her husband. Initially she seldom interacted with other patients.

Her diagnoses included: paranoid schizophrenia and atypical affective disorder with obsessive compulsive features.

Throughout her first year of hospitalization, she continued to be very obsessive. She exhibited a tremendous amount of recurrent thoughts characterized by repetition. As Alice entered the second year of hospitalization, she remained somewhat constricted. Essentially, she was oriented in all three spheres. Her memory was adequate. There was

no evidence of frank psychosis, and Alice denied paranoid thinking. Auditory hallucinations were denied as well. Eating habits were essentially adequate, and there was reportedly no difficulty in sleeping. Alice's insight and judgment remained remarkably unimpaired. One major improvement during the second year of hospitalization was the elimination of self-abusive behavior. Treatment continued to focus on the prevention of self-abusive behavior. Alice's case remained under court review and by early 1989 she was returned to the women's prison since she no longer required a hospital level of care for her own safety and well-being. Her act of self-enucleation had not been copied by other patients or by other female inmates.

When last interviewed . . . Alice expressed the wish that her story would be told so as to assist medical professionals and others in their understanding of self-enucleation.

When last interviewed by authors Halo and Jordan, Alice expressed the wish that her story would be told so as to assist medical professionals and others in their understanding of self-enucleation.

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References

- Gerhard MJP. A propos des automutilation oculaires. Bull. Soc. Ophthalmol.; 68:622-626, 1968.
- Muscovitz RA, Bird T. Rescuing the angel within: PCP related self-enucleation. Psychosomatics, Vol 24:402-406, April, 1983.
- Stewart RM, Jordan TA, Apshaga S. How to write a medical-legal report for litigation with insanity as the defense. RI Medical Journal, Vol 70, 495-497, Nov. 1987.
- Sophocles. Oedipus Rex. Harcourt Brace and World, New York 1939 (Felts D and Fitzgerald R translation).
- Ellis Davidson, HR. Gods and myths of northern Europe. Penguin Books, Harmondsworth, Middlesex, England, 1964.
- Davidson SI. Auto-enucleation of the eye: A study of self-mutilation. Acta Psychother., 10:286-300, 1962.
- Alphen Kok-Van, Volker-Dieben, HJM, Blanksma LJ and Van DenBergh, Automutilation of the cornea, ophthalmological aspects, Documenta Ophthalmologica 52, 327-331 (1982) 0012-4486/82/0524-03270-75. Dr. W. Jenk Publishers, The Hague. Printed in the Netherlands.
- MacLean G, Robertson BM. Self-enucleation and psychosis: Report of two cases and discussion. Archives of General Psychiatry 33:242-249, 1976.
- Tapper CM, Blond RC, Danyluk L. Self-inflicted eye injuries and self-inflicted blindness. The Journal of Nervous and Mental Disease 167:311, 1979.
- Yang HK, Brown GC, Mayarcal LE. Self-inflicted ocular mutilation. American Journal of Ophthalmology 91:658-663, 1981.
- Shore D, Anderson DJ, Cutler NR. Prediction of self-mutilation in hospitalized schizophrenics. American Journal of Psychiatry 135:1406-1407, 1978.
- Feldshuh B, Zasloff M, Froese WA. If thy right eye offend thee: A case of bilateral self-enucleation. Israel Annals of Psychiatry and Related Disciplines 15:145-155, 1977.
- Muscovitz RA, Bird T. Rescuing the angel within: PCP related self-enucleation. Psychosomatics, Vol 24, 402-406, April, 1983.
- Westermeyer J, Serpos A. A third case of self-enucleation. American Journal of Psychiatry, 129:484, 1972.
- Rosen DH, Hoffman AM. Focal suicide: Self-enucleation by two young psychiatric individuals. American Journal of Psychiatry, 128:1009-1012, 1972.
- Eisenhour GL. Self-inflicted ocular removal by two psychiatric inpatients. Hospital and Community Psychiatry 36:189, 1985.
- Cooper SN. Self-inflicted ocular injuries. J All Indian Ophthal Soc 16:213-216, 1968.
- Soria ME, Jordan TA. Clinical prediction of the violent patient, RI Medical Journal, Vol 68:549-551, 1985.
- Matthew 5:29 Holy Bible, King James Version.
- Myths and Realities: A Report of the National Commission on the Insanity Defense: A Project of the National Mental Health Association, Arlington, VA 1983, pp 5 & 6.



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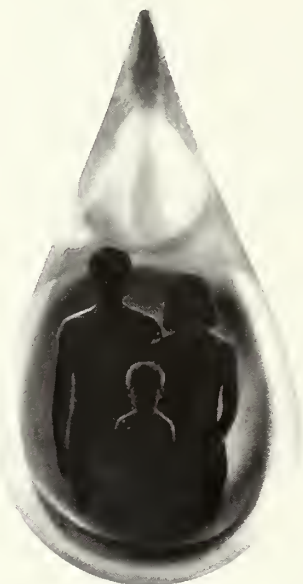
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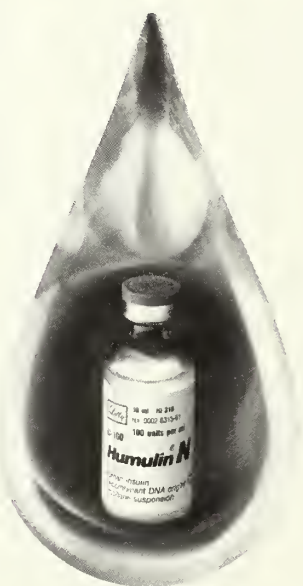
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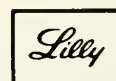


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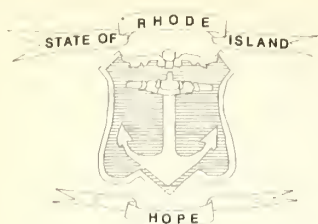
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Mortality from Firearms in Rhode Island, 1980-1987

Over the eight-year period from 1980 to 1987, gunshot injuries accounted for an average of 48 deaths per year among Rhode Island residents. Nearly all of these deaths resulted from the intentional use of firearms: homicides averaged 18 per year and suicides 29 per year. Over the entire period, there were a total of five unintentional deaths and four deaths for which intent could not be determined that were related to firearms.

Guns, including handguns, rifles, and shotguns, were the most common means of committing homicide and suicide during the eight years examined. Forty-two percent of homicides and 27 percent of suicides involved guns. The numbers of firearm fatalities increased over the period, from an average of 44 per year during 1980-85 to 55 in 1986 and 67 in 1987 (Figure 1). Nearly all of the increase was in the number of firearm suicides, which increased from an average of 26 per year over the first six years to 35 in 1986 and 43 in 1987. Homicides and suicides using guns have increased faster than such deaths using other means. During 1986-87, 49 percent of homicides and 33 percent of suicides involved firearms, compared to 40 percent of homicides and 25 percent of suicides during the prior six years.

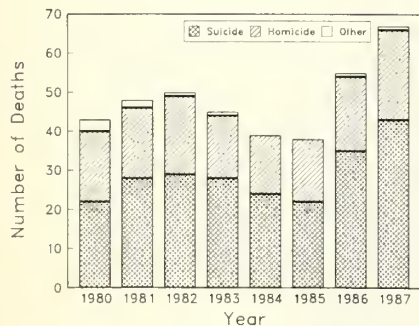


Figure 1. Number of Firearm Deaths by Year and Cause of Death, Rhode Island Residents, 1980-1987

The frequency of firearm deaths differed by age, sex, and race. For both homicides and suicides, persons age 15 to 44 comprised the bulk of the decedents (Figure 2). Firearm suicides were relatively common among the middle-aged and elderly, more so than firearm homicides. Conversely, homicides were relatively frequent among the very young.

Males bore the brunt of mortality from firearms. Of 385 firearm deaths during 1980-87, 326 (85 percent) were males and 59 (15 percent) were females. Blacks, especially black males, were at elevated risk of homicide by gunshot, and white males were most likely to commit suicide using a gun (Figure 3).

Data from Rhode Island and from other areas illustrate the role access to firearms plays in facilitating such events. A recent study of Ohio homicides revealed that a majority of homicides occurred among relatives or acquaintances and most such homicides occurred in households and involved firearms. Of such household homicides, less than half the offenders owned the firearm used, 88 percent involved alcohol and/or drugs, and in 64 percent of cases the gun was routinely kept loaded. A Rhode Island study of occupational mortality during 1979-1984 found significantly elevated suicide rates

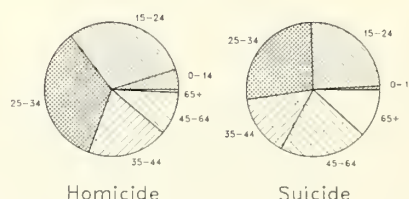


Figure 2. Distribution of Firearm Homicides and Suicides by Age Group, Rhode Island Residents, 1980-1987

among policemen and security guards. Of 16 suicides in this group, 14 involved firearms, to which such workers have easy access. Given that over half of American households possess a gun of some kind, the proliferation of firearms is a public health issue.

References

- Centers for Disease Control. Firearms-Associated Homicides among Family Members, Relatives, or Friends — Ohio. *Morbidity and Mortality Weekly Report* 38:253-6 (April 21, 1989).
- Association of Mortality with Occupation and Industry, Rhode Island, 1979-1984. Providence, RI: Rhode Island Department of Health, Office of Health Statistics (November 1988).

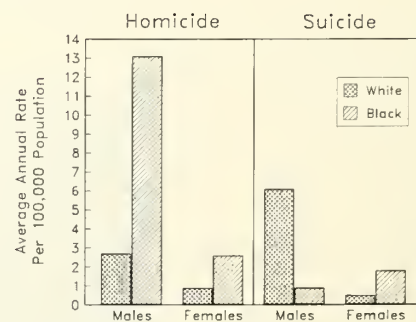


Figure 3. Mortality Rates for Firearm Homicides and Suicides by Race and Sex, Rhode Island Residents, 1980-1987

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with November 1989	
	November 1989 Number	Number	Rates
Live Births	1,131	15,110	15.2*
Deaths	774	9,704	9.8*
Infant deaths	(8)	(154)	10.2†
Neonatal deaths	(4)	(118)	8.2†
Marriages	526	8,188	8.2*
Divorces	256	3,620	3.6*
Induced Terminations	593	7,751	513.0†
Spontaneous Fetal Deaths	68	1,121	74.2†
Under 20 weeks' gestation	(61)	(1,004)	66.4†
20 + weeks' gestation	(7)	(105)	6.9†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with August 1989		
	August 1989 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	288	3,464	348.8	4,350.0
Malignant Neoplasms	206	2,439	245.6	7,602.0
Cerebrovascular Diseases	52	601	60.5	1,026.5
Injuries (Accident, Suicide, Homicide)	31	418	42.1	9,516.5
COPD	23	292	29.4	383.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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HARD CHOICES: Medical Ethics, Law and Health Policy

The Durable Power of Attorney for Health Care: An Important Ingredient of Sound Health Care

Edward N. Beiser, PhD, JD

In 1986, Rhode Island became one of the first states to provide, by statute, for what lawyers call a durable power of attorney for health care. While the title is ungainly, the concept involved is a very simple one which ought to function to the advantage of both patients and physicians. Despite the Legislature's forward-looking action, it is unfortunate that anecdotal evidence from various Rhode Island hospitals suggests that this option is not yet being widely utilized.

The General Notion of Advanced Directives

Contemporary discussions of medical ethics invest considerable importance in patient autonomy. In place of an older view of the physician's role — "Never tell the patient that he has cancer; the doctor will know and do what's best" — it is now widely agreed that the adult, competent patient is entitled to make essential decisions about his or her medical

treatment. Perhaps it is useful to speak now of shared decision-making between the physician (informed by professional skill and experience) and the patient (whose own values become operative). Examples of the respect now accorded to patient self-determination are the practice of obtaining "informed consent" for significant medical procedures, and the notion that a patient may leave the hospital "against medical advice."

If the competent patient is entitled to determine the course of his or her medical treatment, consistent with personal values, what to do when the patient is no longer competent? This may arise either because of a temporary incapacity during the course of an illness, or an irreversible state as in the case of a patient with Alzheimer's disease, or one in a persistently vegetative state.

The reasons which justify following the wishes of a competent patient appear to apply equally even when that patient is no longer able to participate in decision-making. Although a patient, through illness, has lost the ability to articulate his or her values coherently, those expressed patient values rightly continue to determine the course of medical treatment. This then leads to the

idea of prior or advanced directives. Simply put, it is suggested that part of the practice of ethical medicine involves encouraging patients to clarify their preferences while they are able to do so, such that patient values can be respected when the patient is no longer competent to express them.

Living Wills and Durable Powers of Attorney: A Basic Distinction

Two fundamentally different approaches to the notion of advanced directives are currently discussed: living wills and durable powers of attorney. The legal jargon is much less important than the basic concepts involved. A living will is a detailed document through which a patient sets forth his wishes about health care. Just as a conventional will provides instructions about the author's property ("I leave my gold watch to the Rhode Island Medical Society."), a living will attempts to provide instructions to the physician ("I do not want my legs amputated, no matter what.")

One significant objection to living wills is that they tend to be cast in such vague language as to provide little meaningful guidance. Phrases such as "no heroic measures" don't mean much in

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the real world of medical practice. A further significant objection is that clinical decisions are typically complex and subtle; they are rarely "yes or no" choices to be made once and for all. Thus it is difficult for even a sophisticated patient to anticipate in detail the range of treatment options which will be confronted as his disease progresses. There are so many variables, and so many possible choices, that a document purporting to set forth guidance must necessarily be superficial and imprecise.

A different approach, that taken by the Rhode Island statute, is to encourage the patient to identify that person whom the patient best trusts to make his or her treatment decisions when the patient is no longer competent, and then give to that person (called an "agent") the full authority which the patient would have were he or she competent. Instead of saying (as a living will claims to say), "In the event of X, here is what I want done," the patient says, "In the event of X, this is who I want to decide." Instead of attempting to anticipate particular decisions years in advance of their actuality, instead of attempting to anticipate the state of medical technology in the distant future, the patient is asked to identify that relative or friend upon whose good judgment he most relies, and whom he best trusts to reflect his values.

Of particular importance in the execution of a durable power of attorney for health care is the opportunity for the patient to speak at length with the agent about his own values, religious and ethical concerns, fears and hopes. Indeed, the document provided by the Rhode Island statute explicitly includes space for the patient to give limiting instructions to his agent, if he chooses to. The concept is simple: The law in Rhode

Island now allows a competent patient to designate another person who will have the authority to make treatment decisions as fully as the patient would have had, were the patient still competent. The patient's wishes are to be followed. The agent has no power as long as the patient is competent. The patient retains the right to override the agent, or to revoke the power of attorney.

I think that the law is to the great advantage of patients in that it protects patient autonomy as fully as possible, consistent with the realities of medical practice.

I also think that the law is to the tremendous advantage of physicians and hospitals. The statute protects the conscientious physician who wishes to follow his patient's values. It tells doctor and hospital precisely who has the authority to discharge a patient against medical advice, to authorize or refuse to authorize a surgical intervention or to order the initiation or the discontinuation of a treatment modality. The physician or hospital honoring the decision of a properly designated agent need no longer worry about the relative in Chicago (always a lawyer) who hasn't been involved in Papa's treatment in the past but who now threatens to make trouble if his wishes aren't followed.

Rhode Island's Statute

The Legislature has provided a specific form as the exclusive mechanism for creating a durable power of attorney for health care. Most likely this means that other forms of documents claiming to be living wills are invalid. The form provides that the person designated as the agent may not be a treating health care provider, or a nonrelative employee of the treating health care provider or facility. The form need not be notarized but there are important rules regarding the required two

witnesses. In particular, health care providers and their employees may not witness the document. Thus, physicians and nurses should be careful not to act as witnesses. The authority of the agent lasts for seven years, unless a shorter term is provided for. And, as noted above, the form permits the patient to stipulate instructions which limit the agent. For example, a particular patient might say that given his own religious views, artificial feeding should never be discontinued. The statute provides that a court can take away the power of the agent if he "authorizes anything that is illegal, acts contrary to (the patient's) known desires, or where (the patient's desires) are not known, does anything that is clearly contrary to (the patient's) best interests."

Importantly, the statutory form points out that the agent's authority includes, but is not limited to "obtaining or refusing or withdrawing life-prolonging care, treatment, services, and procedures." This language and other aspects of the statute constitute explicit legislative recognition of the authority of a competent patient (or of his properly designated agent) to refuse or discontinue life-sustaining treatment.

What Is To Be Done?

House staff in Brown University hospitals report that they rarely see the durable power of attorney for health care being utilized. This is unfortunate from the point of view of both patients and health care providers.

It is essential that each hospital in Rhode Island develop a set of procedures for determining whether patients have executed a durable power of attorney, for charting that information, and for evaluating whether the document complies with the law. Certainly resident physicians called to a

patient's bedside should not be asked to determine whether a document being shown to them for the first time is legally valid. Each hospital will want to consult its attorney and risk management department as to what procedures will protect both the institution and its patients.

I suggest, finally, that physicians in private practice should routinely inform patients that this opportunity exists in Rhode Island. Certainly in many types of practice it is easily predictable that the patient may become incompetent in the foreseeable future. The physician can gently but

effectively help his or her patients to consider the desirability of clarifying their personal views, and of speaking frankly with loved ones about possible contingencies before they occur. Physicians who have not yet studied the statutory form for creating a durable power for health care (Rhode Island Public Law, Chapter 86-190) may obtain one from their own attorneys, from the Rhode Island Department of Health, or the Rhode Island Department of Elderly Affairs.

Physicians who value the participation of their patients in treatment decisions, physicians whose

professional ethics include a conception of shared decision-making, will want to encourage their patients to make use of the opportunity for providing advanced directives.

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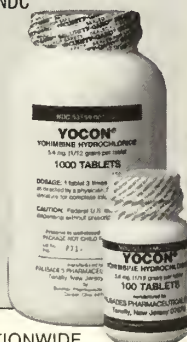
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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (March, 1940)

The lead article is the presidential address given by Harry C. Messenger, MD to the Providence Medical Association. The article notes that "... on the night of January 31, 1848, a few physicians met at the office of Dr H.W. Rivera in Providence, to form a city medical society. We have just concluded the ninety-second year in the life of this Association. Now, with over 500 members, we meet, as did those few, to discuss the medical problems of the day, and as is written in the Act of Incorporation, for 'the advancement of sound medical science and the promotion of the character, interest and honor of the medical fraternity.' " The address discusses committee activities, the inauguration of Blue Cross service in Providence, the efforts to diminish tuberculosis in the urban community, and the idea of creating a volunteer blood donors bureau with a local radio station. The author quotes a professor from a university in a neighboring state who blamed the medical profession for having saved the lives of "hundreds of thousands of debilitated organisms which are adding to the burden of society by reproducing more and worse offspring. Medicine today is an extension of the

maternal instinct mixed up with scientific techniques. It operates in an odor of sanctity and formaldehyde." Messenger derides this attitude and affirms that the purpose of medicine is to treat individuals, to care for the sick and to prevent illness, and to "... let the fuehrers and the supreme commissars do the purging."

R.O. Bowman provides an article on sulfanilamide therapy at Rhode Island Hospital, summarizing all cases which have been treated with sulfanilamide, sulfapyridine or neoprontosil before July 1, 1939. This paper is a summary of an earlier oral presentation given to the W.W. Keen Club of Rhode Island. The article does not indicate the identity of the infective organisms but notes mortality rates of 57% in treated cases of cardiac infection and 50% in treated cases of meningitis. On the basis of a retrospective analysis of 241 cases treated with sulfanilamide, the author concludes: "(1) Therapy with sulfanilamide has been of definite value in the treatment of bacterial infections. It does not work in all cases but a high blood level may give a good result when a low level is of no value. (2) One cannot predict blood levels from the dosage given and the only way to be sure that absorption is adequate for activity is to determine the blood level by change in dosage if indicated. It may be nec-

essary to supplement oral therapy with intravenous therapy in some cases. (3) Low levels are occasionally sufficient to give a good result, and in some cases high levels are still inadequate to combat infection. (4) With decreased kidney function the drug is excreted more slowly. (5) Methemoglobinemia with resultant decreased O₂ carrying capacity and progressive anemia are the two outstanding complications of therapy."

The lead editorial discusses the distinguished and honored role of the renowned surgeon, Dr W.W. Keen, in the American medical profession, noting that Keen was a graduate of Brown University and was a member of its Board of Trustees and a Fellow until his death in 1932. In his honor, a group of young doctors in Providence organized the W.W. Keen Club in 1925. The editorial quotes a letter written by Keen in his ninetieth year describing his personal experience with diverticulitis, a little known disease at that time. Keen, at age 75 (1912), had developed nocturnal diarrhea while lecturing in Berlin. He sailed home as quickly as possible, proceeding to Rochester, Minnesota to seek surgical help from his friend, W.J. Mayo. Two sigmoidal diverticula, one perforated, were discovered and resected. Keen recovered without incident and lived another two decades. (On

Keen's ninetieth birthday [January, 1927], the *Rhode Island Medical Journal* published a commemorative issue honoring him.)

This issue of the *Journal* lists the officers of the Rhode Island Medical Society for 1940. (Charles H. Holt, president; Lucius C. Kingman and Frederic V. Hussey, vice-presidents; Guy W. Wells, secretary; and Jesse E. Mowry, treasurer.) This being 1940, a new standing committee is listed, dealing with matters of "medical defense."

The 1940 treasurer's report of the Rhode Island Medical Society lists total expenses as \$5,887 and total income as \$5,663. Annual dues at this time are \$10.00.

Twenty-Five Years Ago (March, 1965)

The lead article submitted by Alex M. Burgess, Jr., MD, critically examines the practice of news media in associating snow shoveling with sudden death. The author begins with the *Providence Journal* headline of January 15, 1964 which reads, "Blizzard Leaves 11 Dead in State," and points out that one of these 11 was struck by a snow removal truck, one had died of exposure and one died while he was telephoning for help when his car had entered a snow drift. The medical histories of the remaining eight cases were carefully reviewed and the families interviewed. Burgess concludes: "Since in a population the size of Rhode Island's sudden death is almost a daily occurrence, it is not an easy task to decide whether a particular set of circumstances has produced an abnormal number of them. To do so would require a type of investigation which so far has not been satisfactorily done. Furthermore even if we assume that physical exertion of an

acute and unaccustomed sort does pull the trigger and set in motion the mechanism of sudden cardiac death, there remains the possibility that had it not done so, the same medical catastrophe might have appeared hours or days later during some lesser activity, or even at rest. It seems most unlikely that any of the individuals reported here would have survived for long periods merely because of refraining from the particular activity which brought them to journalistic attention. This report does nothing to resolve these difficult problems, but merely suggests suspension of judgment pending better evidence. Since only three of the deaths occurred in cases where there was no known heart disease, since the total number was not demonstrably abnormal, and since other storms which followed were not associated with any such deaths, it seems unnecessary to base any opinion on the impression created by the press report."

A case of infantile cortical hyperostosis is reported by Drs Edward Spindell and Jay Orson, and two cases of eruptive diabetic xanthoma are offered by Drs Ben-cel Schiff and Nathan Sonkin.

A paper is presented by Alfred Fireman, MD describing an extension course in psychiatry for non-physicians. Using the Brown University Extension School Program, 79 adults from the Rhode Island community enrolled in a course designed, "... to recognize mental illness as a disorder with psychological as well as physiological, emotional as well as organic, and social as well as individual effects."

A brief historic paper is presented describing the life and scientific contributions of Dr Henry Bence Jones (1814-1873). This great nineteenth century physician (his London practice included

such personages as Darwin, Faraday and Huxley) is best known as the scientist who applied the principles of chemistry to the practice of bedside medicine.

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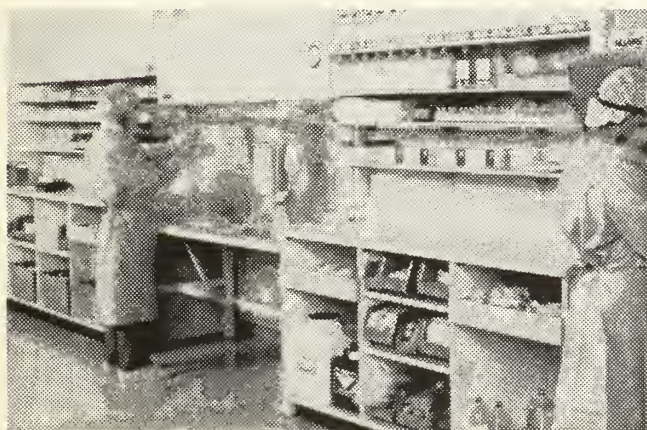
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PHYSICIANS IN THE NEWS

Doctor Edward E. Cureton, Associate Director of Landmark Medical Center's Psychiatry Program, recently attended the Soviet-American Psychiatry Conference in Russia. Focusing on psychopharmacology and biological psychiatry, the conference provided an educational program designed to allow a comparative study between Russia and American health systems. American physicians had the opportunity to visit the Moscow Psychiatric Institute, an outpatient clinic in Leningrad and mental health facilities in several Russian cities.

• • •

The American Board of Psychiatry and Neurology recently awarded board certification in psychiatry to **Doctor Joseph F. Acquaviva**. **Doctor Acquaviva** is a general psychiatrist specializing in anxiety and depressive disorders in adults.

• • •

Recent appointments at Memorial Hospital include **Doctor Alicia D.H. Monroe** as assistant residency director of the Family Medicine Residency Program. **Doctor Wallace L. Akerley, III** has been appointed to Memorial's division of hematology/oncology in the department of medicine.

An endocrinologist at the Providence VA Medical Center and Assistant Professor in the Brown University Program in Medicine, **Doctor Sudhir Bansal** has been awarded a \$121,000 grant to investigate the cause of sexual dysfunction in males with hypertension. **Doctor John Wincze**, Chief of the medical center's Psychology Service and Professor of Psychology at Brown, will be a co-investigator with **Doctor Bansal** on the project.

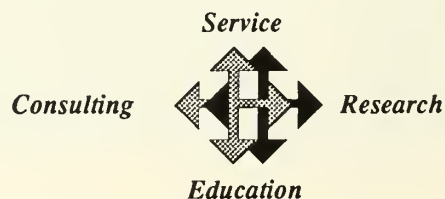
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Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

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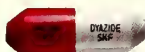
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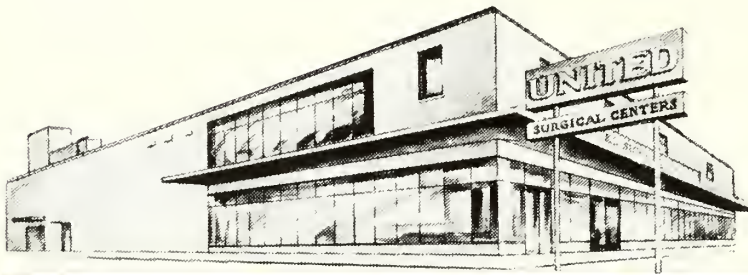
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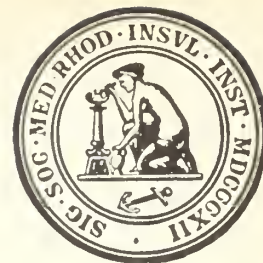
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Volume 73, Number 4 April 1990

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EDITORIALS

Combatting Medical Quackery: Health Professionals' Responsibility, A Symposium

In June of 1989, a group of regulators, educators, advocates and consumers convened a conference entitled *Combatting Medical Quackery: Health Professionals' Responsibility*. The sponsoring agencies included the United States Food and Drug Administration, the Rhode Island Medicine Education Committee, the Rhode Island Consumers' Council, Brown University, the Rhode Island Department of Health, the Rhode Island Pharmaceutical Association, the Rhode Island AFL/CIO, United Way, the United States Consumer Product Safety Commission, and the Rhode Island Department of Elderly Affairs. The one-day conference, held in the Ray Conference Center, Butler Hospital, had a stated goal to "provide information about questionable products and treatments, those agencies to which the provider can report suspect treatments, and most importantly, better communication methods between the health-care provider and health-care consumer." Participants included representatives of the sponsoring organizations as well as the Rhode Island Attorney General's Office, a medical editor of a local television station, and a dietician.

This issue of the *Journal* features three papers selected from the conference proceedings. The papers clearly present the issue

of medical quackery as a big business and mounting problem. Though occasionally so outlandish as to seem humorous, the medical harm to individuals makes this a very real issue calling for serious thought by practicing physicians.

As in so much of medicine, the physician must accept his or her role as an educator if we are to combat this problem. The introduction to the American Medical Association annotated bibliography on alternative therapies, unproven methods and health fraud¹ gives the following sound advice to the health-care provider when the patient discusses a questionable health pursuit:

1. Ask yourself why the person is telling you this story.
2. Hear the person out.
3. Watch your attitude.
4. Be careful what you say.
5. Turn your new insight into a person's motives to that person's advantage in helping them deal with health related anxieties.

It is our hope that these papers will inform and motivate the medical community to combat medical quackery.

Peter A. Hollmann, MD

References

1. Sullivan-Fowler M, Austin T, Wiltafner A: Alternative Therapies, Unproven Methods and Health Fraud: A Selected Annotated Bibliography. AMA Division of Library & Information Management 1988;2.

New England's Patent Medicines

This issue of the *Journal* discusses medical quackery, particularly as it persists in Rhode Island. 'Quack' is a curious bit of jargon, defined usually as a pretender to medical skills and one who boasts of access to wondrous cures. Its origins are found in the sixteenth century Dutch word, *quackzalver*, the German cognate, *Quacksalber*, and the English, *quacksalver*, all meaning a person who boasts [quacks] about the merits of his salves [ointments].

In usage, 'quacksalver' was quickly abbreviated to 'quack' as the noun describing a medical charlatan or mountebank. Charlatan carries a somewhat broader meaning suggesting more an unscrupulous salesperson, the word rooted in the Italian, *ciarlatano*, a babbler or prattler. The origins of mountebank are also found in the Italian, *montambanco*, an itinerant charlatan who mounts a bench when selling his wares.

As literacy advanced in nineteenth century New England, roadside leaflets and newspaper advertisements replaced the human voice as the persuasive medium for health care fraud. The current problems of medical quackery in Rhode Island are not, therefore, the itinerant charlatan or the individual mountebank dispensing snake oil from the back of a wagon. Rather, the danger lingers in the various advertising media which now hawk unproven, worthless, and even occasionally harmful, health care products.

New England has contributed materially to the lore of medical quackery. During the nineteenth century some of the leading purveyors of worthless medications started their operations in this region. Neither the content nor the claims of their patent medicines were subject to any external regulation. Their 'active' ingredients were often extracts of celery, sarsaparilla or coca leaves. Virtually all contained substantial concentrations of ethyl alcohol explained as a necessary solvent for the vegetable extracts and as a means of preventing the medication from freezing in the winter. Few of these original nineteenth century compounds have survived but their memory still persists in carbonated drinks containing celery tonic, sarsaparilla and the colas.

Sarsaparilla (*Aralia nudicaulis*) was introduced during the early years of the last century as a "natural remedy" for the undefined ills and sluggishness experienced during early springtime. It was advocated as a tonic to counteract fatigue, to purify the blood and to cure numerous chronic ailments and infections. In 1841, James C. Ayer, a newly graduated physician, purchased a small pharmacy in Lowell, Massachusetts and invested his energies and funds in a line of home remedies. The Ayers' Extract of Sarsaparilla became the most famous and profitable product of his pharmaceutical factory, at its peak manufacturing in excess of 600,000 doses daily. The formula, according to its label, contained the following substances in a fluid base of 21 percent ethyl alcohol:

fluid extract of sarsaparilla	3 oz
fluid extract of stillingia 3 oz
fluid extract of of yellow	
dock 3 oz
fluid extract of May apple	.. 3 oz
sugar 1 oz

potassium iodide90 gr.
ferric iodide10 gr.

Ayer's entrepreneurial and managerial talents were legendary and his enterprises prospered. He became one of Lowell's most respected and wealthy citizens. Upon his death, the nearby Massachusetts town of Ayer was renamed in his honor. Despite these successes, none of the botanical compounds used in the various sarsaparilla formulations have ever been found to have any therapeutic value except for those competitor celery tonics containing the cathartics, cascara and senna.

No historic or mythologic evidence exists to suggest that extracts of celery contain agents which strengthen the brain and nerves. Wells and Richardson, Civil War veterans whose business zeal brought them to the wholesale drug business, nevertheless began to manufacture a celery compound, the formula for which they had purchased from a Vermont widow named Mrs. Paine. Through the genius of advertising [particularly in free pamphlets distributed in New England drug-stores] their Paine's Celery Compound emerged as one of the leading proprietaries for "nervous diseases" in the United States. The compound contained 21 percent ethyl alcohol as well as some celery tonic, hops and coca. The manufacturers were particularly proud of the coca content and proclaimed that this was the very same product which South American Indians chewed to provide them with unusual strength and a means of forgetting their misfortunes.

In 1843 a young school teacher in Lynn, Massachusetts, Lydia Estes, married Isaac Pinkham. She resigned her teaching position, leaving to her husband the duties of supporting the family. In one

of his many failed business ventures, he was left with a vegetable-based remedy described as a cure for the ailments of females. His wife Lydia assumed responsibility for the formula, modified it somewhat in her kitchen and dispensed it periodically, without fee, to family and neighbors. Its commercial utility was not appreciated for years, but when finally Lydia E. Pinkham's Vegetable Compound was marketed, now fortified by 18 percent alcohol, its sales brought it to the forefront of patent medicines. Through creative advertising the compound found a ready and eager market throughout the United States and in virtually every country accessible to commercial shipping. This herbal compound used for a spectrum of "female complaints" became a household necessity in millions of homes and a symbol of reliant self-help in a culture which regarded organized medicine with much skepticism. Lydia Pinkham died at age 62 but her patent medicine lived on for many more decades and her name became synonymous with Mother Nature's bountiful health aids.

By the onset of this century, America was witness to increasing numbers of fraudulent and occasionally harmful products flooding its unregulated marketplace. Many were laced with various opiate and coca-leaf alkaloids and alcohol was the near-universal diluent. The names of these proprietaries remain in faded barnside advertisements, attic magazines and history texts, names such as swamp-root compound, Kickapoo Sagwa [first sold in Providence, RI], Pitcher's Castoria, little liver pills, Warner's Kidney Cure, Hadacol, Katonka, and the various Universal Balms. Congressional investigation of the patent medicine industry, during the first decade of this century saw Rhode Island's Senator Nelson

Aldrich resolutely opposing the enactment of the Federal Pure Food and Drug Act, while the American Medical Association, and its membership of 135,000 physicians, urgently demanded its passage. The AMA position prevailed and the bill was signed into law by President Theodore Roosevelt in 1906.

The many recent advances achieved by medicine cannot hide our residual inabilities, particularly in curing chronic ailments of the elderly. Human credulity and these therapeutic limitations become the two fertile substrates for those who seek quick miracles and for those who would exploit such persons.

Stanley M. Aronson, MD

Response to Editor's Mailbox: RIMJ, March, 1990

Re: Detoxification of the Chemically Dependent Patient

I greatly appreciate your kind comments on my paper on detoxification of the chemically dependent patient, and I would like to comment on your concerns about the lack of facilities for detoxification of indigent patients. A very substantial number of patients presenting for detoxification to Emergency Departments do not require medical detoxification, and could be managed in a social-setting detoxification program. It is clear that there is a need for increased beds at this facility, and probably the creation of similar facilities in other parts of the state. Such social-setting programs can be operated at substantial savings over medical facilities, and can provide safe and effective services for patients, in-

cluding referral to rehabilitation programs. I support your efforts to alert public officials to this need. Many of us who work in the field of chemical dependency have repeatedly communicated this point to the same officials.

I am concerned, however, at the concept that indigent patients with a need for medical detoxification should be referred to some other facility as a matter of course. I know of no other medical condition where the patient's level of insurance coverage should dictate whether they are admitted to a hospital when they present to an emergency department. As the internist in charge of admission to a hospital-based detoxification and early treatment program, I frequently communicate with area Emergency Service physicians. I have been involved in cases where patients who are intoxicated and have medical or psychiatric problems which might render detoxification dangerous or even lethal are sent out of Emergency Rooms without treatment, because my facility did not have an available bed, and the State facilities were, as usual, fully occupied.

I do not understand why alcoholic and other chemically dependent patients should be refused care, and why hospitals do not accept the responsibility of providing that care. There are no longer leprosaria and tuberculosis sanatoria, but there still appears to be a need for similar out-of-the-way places in which to hide our chemically dependent. The care needed by these patients is neither so specialized nor complicated as to require such referral, except in extraordinary cases. The underlying problem is the negative attitudes so often prevalent in health professionals towards these patients, and the lack of training and knowledge base in the addictions in medical and

nursing schools. That negative stereotypes are often reality-based, that many of these patients can be difficult and disagreeable, does not justify the abrogation of our professional responsibilities towards them.

I do agree that additional facilities for both social setting and medical detoxification are needed. I would like to see our hospitals recognize their own responsibility in this area, and help train their staff in the management of the chemically dependent, so that attitudes, skills and behaviors can be altered to provide improved care. There is a drug epidemic (which includes alcohol) in America. It will not be solved by a fortress mentality in which the victims of the epidemic are relegated to the modern equivalent of Bedlam. The "not-in-my-backyard" (NIMBY) mentality extends to hospitals as well as to neighborhoods.

Alan A. Wartenberg, MD, FACP
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Combatting Medical Quackery: A Message to the Physicians of Rhode Island

H. Denman Scott, MD, MPH

It takes an effort of will to recognize that medical quackery today is big business . . .

As Director of the Rhode Island Department of Health, I am grateful to the *Journal* for the opportunity to share my views concerning a significant health issue, medical quackery.

As you might expect, I view the problem from a double perspective: that of the clinician and that as the Director of Health for the state. The issues are essentially the same from either view, but not necessarily the conclusions, especially about the responsibility of health professionals in controlling these abuses. At the heart of this distinction is the classical question: To what extent are the broader social goals of medicine the responsibility of individual physicians in their daily practice? I hope that my comments will serve to encourage you to adopt the conviction that practicing physicians have, indeed, both the opportunity and the responsibility to combat medical quackery.

The View From Private Practice

From the beginnings of organized society, in all known cultures, there has been an impulse to seek the help of "healers" to cure ill-

H. Denman Scott, MD, MPH, is Director of the Department of Health of the State of Rhode Island, Providence, Rhode Island.

ness, repair injury, control pain, enhance beauty, assure fertility, delay death. In some cultures the healer has adopted the attributes of priest; in others, magician; in still others, wise student of nature and the body. But the impulse to seek help has been constant and remains with us still. Some of the older attitudes towards the physician as "healer" persist today coexisting with the more evolved perceptions of the health profession.

During the last two hundred years, however, tremendous advances have been made in scientific medicine, greatly enhancing our diagnostic and therapeutic skills. Equally significant, the rise of scientific medicine and experimental design has enabled us to distinguish between therapies which work and those which do not. And while this new ability has now allowed us to define the unsafe, the ineffective, and the fraudulent, it has certainly not eliminated medical quackery. Indeed, the public continues to patronize quacks as an alternative to modern medicine, and sometimes to patronize both quackery and scientific medicine simultaneously in seeking treatment for the same ills.

Physicians are taught that their first obligation to the patient is to "do no harm." This is a sound precept. It is also a conservative

one. But do not physicians and other health professionals also have an obligation, when they see their patients pursuing a harmful course of self-treatment, to advise them to desist? In theory I think we would all agree, but in practice many of us do not. Why do we hesitate to intervene? And why, so often, do we avoid the proactive role? If quackery persists, is it not with the tacit complicity of physicians, nurses and pharmacists? We must understand the basis for this complicity if we are to alter our approach.

Partly, I think, we are prisoners of a semantic heritage. The very term which we use for this medical abuse — quackery — has a vaguely comic sound, due perhaps to some subliminal association with the antics of Donald Duck. There is, thus, a tendency for us to underrate its seriousness. Yet quackery is a very serious business indeed with tremendous health and monetary implications for society.

The Oxford Dictionary defines a quack as: "An ignorant pretender to skill, especially in medicine; a charlatan." Many of us still define quackery as the pretensions of a misguided individ-

Abbreviations Used:

FDA: US Food and Drug Administration

ual who believes in his unique powers or nostrums, or alternatively, the cynical entrepreneur selling snake oil from the back of a medicine-show wagon. It takes an effort of will to recognize that today's quackery is big business, the commercial exploitation of human frailties, wishful thinking, gullibility, hope, and despair. There is a great deal of money to be made from the countless human dramas of failed expectation, and not a few corporate empires are based on the heartless pursuit of profits from this source. Useless and even dangerous products have superceded "ignorant pretenders to skill" as the largest part of the problem.

Then, too, health professionals have an understandable reluctance to interfere in the private lives of their patients if they believe that the patient will resent such interference. Physicians are wary of seeming to condemn a competing source of care, for fear of drawing the charge that they are only trying to maintain a profitable monopoly.

At the height of the McCarthy era, one of the characters in Walt Kelley's *Pogo* says, in resisting the officious efforts of government to "protect" him, that in a democracy the people have a "right to make damn fools of themselves." We are all, physicians and patients alike, the captives of this democratic ethos.

Physicians are wary of seeming to condemn a competing source of care, for fear of drawing the charge that they are only trying to maintain a profitable monopoly.

There are doubtless instances in which the practitioner says, in effect, if it makes patients happier

to try unorthodox therapies, why not let them do so as long as they aren't clearly injurious? We are a nation given to health fads: diets, folk remedies, exercise programs, pills. Since it is not always clear initially whether a fad is helpful or harmful, the medical practitioner customarily withholds comment.

The View From a State Health Agency

Public health agencies exist to deal with those societal problems which cannot be addressed effectively or assertively by individual health professionals. Food and drug legislation, at both the federal and state level, comes under this heading.

The US Food and Drug Administration (FDA) has a national mandate to assure the safety and efficacy of prescription drugs. The Rhode Island Department of Health has a legal mandate (Chapter 31 of the Rhode Island General Laws) to prevent the sale of food, drugs, medical devices or cosmetics which are adulterated or misbranded. The existence of public authorities with mandates in these areas does not relieve individual health professionals of *their* responsibilities. Indeed, without the active support of individual medical practitioners, public authorities are hampered in fulfilling their assigned mission.

We have established a very successful program in Rhode Island which encourages physicians to report adverse drug reactions to the FDA. This program was initiated, with federal funding, because physician cooperation is essential to a continuing community monitoring of approved drugs. Yet there is irony in a situation whereby physicians report adverse reactions to medications which they have prescribed but they remain silent in

the face of widespread use of quack therapies by patients under their personal care.

The Rhode Island Department of Health has a legal mandate . . . to prevent the sale of food, drugs, medical devices or cosmetics which are adulterated or misbranded.

Let me share with you some examples of quack products which have been marketed in Rhode Island over the past few years:

- So-called "natural will power" weight-loss systems using bran pills and starch blockers.
- Unapproved drugs such as Laetrile promoted as cancer cures.
- Vitamin combinations promoted as hair restoratives.
- So-called oral tanning tablets, also known as sun tan pills.
- Products labelled as steroids, but not really drugs of the steroid/anabolic class, sold in connection with muscle/building programs.
- A variety of unproven products promising relief for arthritis pain.
- Products promoted as wrinkle removers, bust developers, or sexual aids.
- Dermal patches guaranteed to cause weight loss.

Why should physicians be concerned about these products, especially those which are directed toward vanity objectives of the consumer? Do they really constitute a health problem? The answer is assuredly yes.

We are concerned about the safety of any drug or device which is promoted for health purposes. We are probably more concerned with over-the-counter and mail-order products than prescription drugs because so little is really

known about many of them, particularly their chemical composition, effects of long-term use or high dosage, and potential for adverse interaction with other drugs.

... physicians report adverse reactions to medications which they have prescribed but they remain silent in the face of widespread use of quack therapies ...

We are concerned about any unorthodox product, device or therapy for serious illness which might delay a patient's seeking medical care or using proven therapies.

We are concerned about false claims made for health products, even when relatively harmless, because fraud should have no place in the health industry.

Under Chapter 31 of the General Laws, Rhode Island Food, Drug and Cosmetic Act, the Department of Health is empowered to identify and embargo:

- poisonous or deleterious substances,
- adulterated drugs or devices,
- misbranded drugs or devices, including those labelled in a false or misleading manner, and
- new drugs not yet determined to be safe and effective.

Embargoed products may not be sold pending a court hearing. If the court finds that the embargoed products are in violation of the law they are destroyed. The Department enforces these provisions on a continuing basis, usually in cooperation with the US Marshall's Office and the FDA, Division of Drug Control.

There are limits to the reach of our authority. For example, the State cannot control misleading advertising which enters the state

in publications or over cable TV; furthermore, the enforcement capabilities of the State is limited by the small staff assigned to this function. A very significant limitation is the Department's inability to provide direct counselling to individuals in their personal health strategies. This is true not only of quack products and therapies, but also of unorthodox therapies which are not inherently dangerous or useless, but may be wrong for them. These are areas where the involvement of the individual health professional becomes essential.

* * *

It is my hope that a realization of the responsibility of Rhode Is-

land health professionals in combatting medical quackery will lead to their increased commitment to: (1) better control of dangerous and useless products, and (2) more aggressive counselling of their patients concerning non-prescribed remedies. The Rhode Island Department of Health stands ready to participate actively in a strong community effort directed towards these ends.

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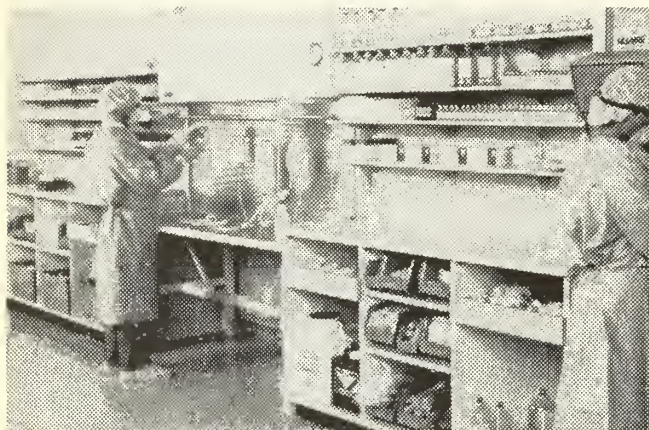
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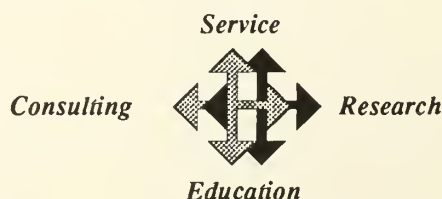
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Medical Quackery in Rhode Island: The Perspective of State and Federal Drug Control Agencies

Paula B. Fairfield

Charles Hachadorian, Jr, MPA, RPh

... it was a quack cancer treatment which led Congress to enact the first federal law against false claims for drugs.

Health fraud or medical quackery is the promotion, for profit, of medical remedies known to be false or unproven. This is usually accomplished by falsely representing certain products, goods, or alleging them to be of aid in the cure of various diseases. Quackery has existed throughout history.

Today, few people remember that it was a quack cancer treatment which led Congress to enact the first federal law against false claims for drugs. The congressional intention was that the 1906 Pure Food and Drug Act would do away with the thousands of useless and dangerous patent medicines on the market, but health fraud has remained alive and well. Present estimates say that be-

tween 10 and 40 billion dollars a year are being spent on bogus products. Remedies are still being advertised which make all sorts of promises, but fail to work. Those who invest their hard-earned money in these worthless products at the very least will experience both helpless anger and frustration.

Most consumers are not in a position to take legal action against promoters of health fraud, or even to know what action can be undertaken to protect themselves. Health fraud is just as prevalent today as yesterday, and because litigation is significantly more expensive, public impotence continues to be a major problem. Therefore, Federal and State programs must focus attention on this issue. The volume of this and other problems in their jurisdiction necessitates a priority classification system. Priority classes in descending order are:

1. *Direct Health Hazard* — These are products that can harm the user's health, or even cause death. Whatever actions are necessary to remove these products from the market have top priority.

2. *Indirect Health Hazard* — These are ineffective products which, while not causing the user any direct harm, may delay or

even replace proper medical care at a time when it is needed.

3. *Economic Fraud* — These products are either useless or useful products labelled with additional unsupported claims. They pose little or no health risk but cheat consumers out of dollars spent futilely.

The FDA's Boston District Health Fraud Survey

One initiative by the local office of the FDA has been to search regional and national publications in order to monitor health fraud, comparing local products to those promoted elsewhere and to note changes in the nature of fraudulent claims. This search has been ongoing for three years.

Promotions for body-building products or devices and anti-aging agents rose notably during the survey period. Numerous products were identified through the search and removed from the

Paula B. Fairfield is with the Federal Food and Drug Administration Regional Office, Consumer Affairs Office, Stoneham, MA.

Charles Hachadorian, Jr, MPA, RPh, is Drug Control Administrator with the Rhode Island Department of Health, Division of Drug Control, Providence, Rhode Island.

Abbreviations Used:

AIDS: acquired immune deficiency syndrome

DMSO: dimethyl sulfoxide

FDA: Food and Drug Administration

GH3 rejuvenators: anti-aging products

market or seized. An area receiving priority is the removal of unproven immune booster products aimed at AIDS victims. Two Connecticut firms were referred to the Postal Inspection Service and are now out of business. One firm was selling Big Bosom Tablets and the other a product to dissolve varicose veins. Inspection by the FDA found the companies to be one and the same.

One of the district office's activities is to send letters to local publishers of newspapers when an advertisement for a fraudulent product has been found. The letter requests that the publisher not print advertisements for such products, thereby doing his readers a public service. It also offers the services of the Consumer Affairs Office of the FDA in reviewing ads. Response has been varied. One publisher called and said that he is in business to make money and if the FDA felt the products were frauds, why didn't the FDA take out an advertisement saying so. Several publishers called saying they did not realize the products were frauds and would be more careful in the future. Others made no response.

The Boston District Office plans to continue its annual literature survey in order to identify the ever-changing profile of health fraud in New England, to use the information compiled during the survey to respond to inquiries about new product promotions, and to select targets for appropriate regulatory and administrative follow-up.

Rhode Island Drug Control

The Division of Drug Control, within the Rhode Island Department of Health, is responsible for the enforcement of the Food, Drug and Cosmetic Act. Marketing of products in the United States requires Food and Drug Administration approval at the federal

level, and marketing within Rhode Island requires the approval of the Director of Health. The Division represents the Director in matters of safety and effectiveness of new drugs, and for those currently in commerce. The Director is also responsible for post-marketing drug surveillance, and for matters of drug product selection and generic equivalence. It is the responsibility of the Director to protect the people of the State from products that are deceptively labelled, that are fraudulent, that are misbranded or adulterated, or falsely claim to prevent or treat diseases, or otherwise effect structures or functions of the human body. For these regulatory purposes then, these products are considered to be drugs, cosmetics or devices.

The Director of Health, state of Rhode Island, is . . . responsible for post-marketing drug surveillance, and for matters of drug product selection and generic equivalence.

One of the most widely publicized cases in Rhode Island history involved the importation of Amygdalin, as Laetrile, into Rhode Island. Attention was gained because legislation was introduced which would have exempted this product from the Rhode Island Food, Drugs and Cosmetic Act, and therefore from enforcement by the State Division of Drug Control. Control under the Federal statutes would have been effective but the issue became one of convincing State legislators that the regulatory process for safe and effective drugs was necessary to protect the public health.

Agents of the Division of Drug Control have embargoed and/or seized vitamin B-15, ginseng, so-called natural steroids, DMSO, as

well as other products used in muscle-building and increasing weight gain and body density. These products are widely sold in health food stores throughout the state.

Vitamin B-15, or Pangamic Acid, has been the subject of FDA action for many years.¹ There have been Food and Drug Administration import alerts because there is no vitamin recognized as vitamin B-15. It is being promoted as safe and effective for use in the cure, mitigation and/or treatment of a variety of diseases, including heart disease, peripheral vascular disease, diabetes, cancer, liver disease, asthma, emphysema, and alcoholism. The Division of Drug Control embargoed these products as being misbranded. It should be noted that Ernest Krebs, Jr, the originator of vitamin B-15, was also the originator of Laetrile. Despite the fact that it has been declared nutritionally useless, and that the United States government has stated that it is illegal, worthless, and possibly unsafe, it is still widely promoted in health food stores in Rhode Island.

Agents of the Division of Drug Control have embargoed and/or seized vitamin B-15, ginseng, so-called natural steroids, DMSO, as well as other products used in muscle-building and increasing weight gain and body density.

Dimethyl sulfoxide, or DMSO, presents a special problem. It is approved by the Food and Drug Administration for interstitial cystitis, with proper warnings concerning cataract formation. When DMSO is sold in hardware stores as an industrial solvent, there are no problems with misbranding or mislabelling. If however, physicians, pharmacists, or others rec-

commend or vend the product for indications for which it is not legally approved, it is subject to the same embargo as any other misbranded drug.

The desire to lose weight, grow hair, and be free from wrinkles is all part of the "Fountain of Youth Syndrome." Many of the legitimate department store chains that are nationwide, will advertise wrinkle creams using a pharmacist or other health professional as a spokesperson.² However, the spokesperson may not necessarily be expert in the biology or pharmacology of the conditions and treatments at issue. Knowledge in one area is often capitalized upon in a promotional effort for a product in an unrelated field.

During 1987 and 1988, tanning salons in the State of Rhode Island offered skin patches for diet control. Millions of dollars worth of so-called "Diet Patches" were seized as the newest weight-loss gimmick. Tanning salons were visited by agents of the Division of Drug Control, and the product was embargoed. On June 24, 1988, the Division of Drug Control assisted the Nutrition Service with a press release warning Rhode Islanders that diet patches now being marketed in the state did not have approval by the Federal Food and Drug Administration. The press release went on to say that these patches mimic legitimate prescription transdermal patches used to deliver drugs to the skin for such conditions as motion sickness. "No non-prescription patch delivering drugs or other substances through the skin has been approved by the FDA."³

With the spread of the AIDS virus, there arises another class of desperate individuals seeking cures who may fall for fraudulent remedies. These remedies now include the processed algae, injections of hydrogen peroxide,

food preservatives, and herbal capsules that were found to contain chlorine bleach solution as a wash, and injections of processed by-products of the patient's own urine.⁴

It is understandable that patients suffering from terminal diseases such as AIDS might look to macrobiotic diets, massive doses of vitamin C, body cooling with deionized water, ozone therapy, or all the other scams currently being perpetrated. However, the relatively small AIDS population could not account for the billions of dollars spent on quack products. The teas, starch-blockers, the body wraps, the hair growers, the youth cures, the GH3 rejuvenators, the liquid protein diets, and all the rest, depend upon for their existence, the convincing of a large audience to buy. It is the duty of all health professionals to report these frauds, and to assist

the appropriate agencies in vigorous prosecution. This is done without preventing the study of new, albeit unconventional, therapies. It is done to protect the public health.

References

- ¹ "Vitamin B-15," *The Informer*, University of Rhode Island, College of Pharmacy, Information Service, Vol. 3, No. 6, Nov-Dec, 1979.
- "Pangamic Acid," Food and Drug Administration Talk Paper, 24 November 1980.
- "Vitamin B-15," Publication of the Idaho Board of Pharmacy, 9 June 1980.
- "Memorandum," FDA Policy, 20 July 1987.
- "FDA Seizes Vitamin B-15," *Drug Topics*, 6 March 1981.
- "Vitamin B-15 Sales Blocked," *FDA Cosmetic Law Journal*, Vol. 33, No. 4, April 1978.
- "Talk Paper," Food and Drug Administration, 31 March 1978.
- Food, Drug and Cosmetic Law reports, paragraph 42,230.
- ² "Peddling the Fountain of Youth," Samuel D. Uretsky, *American Pharmacy*, No. 12, December 1985.
- ³ "Talk Paper," Food and Drug Administration, 11 May 1988, 17 June 1988.
- ⁴ "Defrauding the Desperate: Quackery and AIDS," *FDA Consumer*, October, 1987.

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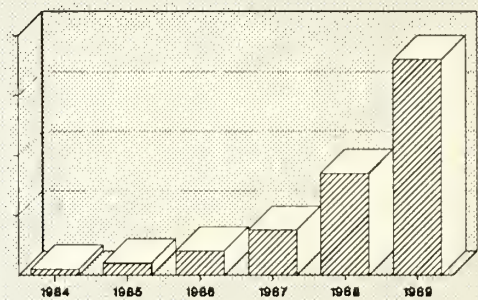


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Quackery and the Elderly

Peter A. Hollmann, MD

Whether or not older persons are more likely to fall victim to quackery, it seems certain that they are more likely to be harmed by quackery.

Elderly persons are often viewed as being at special risk for various fraudulent schemes. Not only are they more easily victimized, but they are more severely harmed when so victimized. Statistics concerning medical quackery exploiting this age group are cause for legitimate alarm. Estimates indicate that while the elderly comprise but 12 percent of the population, they now represent almost 40 percent of the health-fraud victims.¹ Lest such a conclusion be regarded as an inherently ageist characterization, we are obliged to assess more critically this vulnerability of the aged to health-care fraudulence.

It must be appreciated that 'the elderly' is a term which describes a widely varied population. Indeed, one of the hallmarks of aging is the acquisition of diverse biological, behavioral and social traits. It is equally true that older individuals are members of a greater society, and are not isolated from the trends of their era. However, in considering risks, it is not inappropriate to make gen-

eralizations about groups, understanding the limitations of this in consideration of the individual.

Quackery has been with our society always. This has been the case despite significant increases in the average person's understanding of medical science and dramatic changes in that science itself. While there is little empiric data as to why individuals seek care from fraudulent providers, several motivating or facilitating factors have been suggested.

Motivating Factors

First, there is the perceived benefit. The tendency to embrace unproven therapies is stronger when the affliction is incurable or life-threatening. Therefore, diseases such as the Acquired Immune Deficiency Syndrome or Alzheimer's Disease are more likely foci of a product's promotional strategy. Other chronic conditions such as arthritis are also good targets. Furthermore, diseases with naturally occurring remissions, such as the chronic musculoskeletal afflictions or multiple sclerosis, are particularly susceptible to a placebo effect. A second important factor is a willingness to consider alternative therapies. This could stem from a cynical skepticism of traditional medicine, gullibility, or merely a genuine open-mindedness. The quack

seeks business from diverse groups and alters his sales pitch to appeal to selected audiences that are willing to listen. Both the individual seeking a miraculous cure from a potent healer or the educated, prevention-minded partner in health care seeking to take control of his or her body, are potential targets for the quack.

Age has the potential to alter selected risk factors for quackery. It remains debatable as to how much physiological decline is due to normal aging, but it is not controversial that the aged are more likely to have disease and functional impairment than their younger counterparts. Four of every five community-based persons over 65 years of age have at least one chronic disability. For example, 46 percent of the elderly have arthritis and 28 percent have a hearing impairment. Arthritis, hearing impairments, hypertension, and heart conditions, together account for approximately 60 percent of all chronic disease in this senior population. In each case, the prevalence of these conditions is at least fivefold greater than that of an under 45-year-old

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*Abbreviations Used:
OTC: Over the counter (medications)*

cohort.² More than 50 percent of the cancers occur in the elderly and 5 percent suffer from severe dementia. Forty-four percent of those over 85-years-old require personal care assistance. The great majority of illness in the aged, indeed, is chronic.

Four of every five community-based persons over 65 years of age have at least one chronic disability. For example, 46 percent of the elderly have arthritis and 28 per cent have a hearing impairment.

Older persons use health services at a greater frequency than their younger counterparts. They account for 39 percent of all acute hospital days and 30 percent of the prescription drug use. Despite this, knowledge of illness reporting and steps taken for health problems suggest this high use represents a surprisingly uncommon option of the elder person when faced with an illness. Nearly 90 percent of individuals interviewed in one survey had experienced symptoms of illness in the previous month, but nevertheless continued to report their health in positive terms.³

Individuals over 75 years, while acknowledging more disability than the 65-74 year old group, tend to describe their health as better.³ Self perception of health is also related to the extent to which health services are employed.

Young and old tend not to consult a physician for the great majority of their health complaints. The behavior of the elderly is of interest, however, in terms of their likelihood to expose themselves to unorthodox or improper care. When a *defined* health problem arises, the elderly will seek the advice of a physician approxi-

mately 10 percent of the time. They will use a home remedy with equal frequency. This is distinct from the use of a nonprescription drug which is depended upon one-third of the time. Roughly 15 percent of the time a prescription that is at hand is used and in one-third of instances, the symptoms are not treated at all.⁴

The elderly consume approximately one-third of the nation's health resources, be they traditional or unproven remedies. Therefore, it could be argued that the elderly are no more or less susceptible to quackery than they are to scientific medicine. This supports the hypothesis that medical need, more than an age related propensity to be victimized, contributes to the probability that help will be sought from a quack. It is apparent that the use of home remedies or nonprescription remedies is a very common behavior in response to illness. It also is the case that traditional and unorthodox therapies are used concurrently.

While over-the-counter (OTC) drugs would not properly be considered products of quackery, understanding their use sheds light upon the problem of quackery. The advertising claims of OTC drugs have bordered on quackery at times and, upon occasion, have crossed over that border prompting governmental intervention.

A perusal of the shelves of a 1990s corner drug store will reveal a wealth of "Maximum Strength," "Special Formula" products that promise fast relief, at least in most cases. They will cool or warm deeply or do both at once. Energy will be restored and appetites controlled. "United States Medical Expert Advisory Panels" vouch for safety and efficacy. While physicians may not be impressed with the maximum power of a 500mg tablet as compared to a 325mg tablet or by that

special formulation of caffeine or acetaminophen, it is very tough to argue with the sage advice on the box of one product. It reminds hard-drinking, fad-dieting, chain-smoking, physically-stressed persons that a good diet, preferably reinforced by the particular vitamin contained inside the package, is important.

While the government and manufacturers have gone to considerable lengths to provide for safety warnings and instructions on proper usage, a study of respondents over age 65 years found that the surveyed individuals could not or did not read the required labels on OTC drugs.⁴ The most common source of information about OTC drugs was their advertising claims. It was the source depended upon twice as frequently as the interpretation offered by the pharmacist. Advice from friends, relatives, or neighbors was the second most common source of information.⁴ Of course, the source of information varies according to the nature and magnitude of the health problem. For example, a physician's advice is often sought for arthritis products, but much less likely for bowel regularity remedies.⁵

The tendency to embrace unproven therapies is stronger when the affliction is incurable or life-threatening.

Numerous other issues may be pertinent in comparing the elderly to the young in terms of vulnerability to quackery. Older people are more likely to accept the authority of physicians than are the young. Does this make them more readily the passive victim of a quack or less cynical about traditional medicine and therefore less likely to seek alternative therapies? Older individuals tend to

have good health-promoting behaviors. Does this make them less likely to rely upon a pill or tonic or more likely to stay healthy by taking prevention-oriented, "natural" health products? Here, there may be an impact based upon the number of hours exposed to media with less expensive advertising costs where advertisements for fraudulent products would customarily be placed, magazines or radio advertisements, as compared to television. Lessened mobility may also affect the probability of the patient's use of mail-order products.

The elderly's integrity as bill payers probably make them a more appealing target. The experience of witnessing sixty years of medical miracles may make patently ludicrous claims seem plausible to the elderly who may also have fewer numbers of years of formal education. However, the significance of these generational differences is neither known nor intuitive.

Whether or not older persons are more likely to fall victim to quackery, it seems certain that they are more likely to be harmed by quackery. The high incidence of serious, adverse drug reactions and the correlation of this incidence with age, puts the elderly at greater risk from the direct negative effects of fraudulent treatments. The higher prevalence of serious, but treatable disease in the elderly places them at greater risk of being victimized by the indirect negative effect of delayed or missed proper diagnosis and treatment.

The Role of the Physician

Physicians play a major role in combatting quackery. The manner in which a geriatric patient is treated is significant in this regard. Principles of good geriatric medical care apply. The physician who responds to health con-

cerns with "What do you expect for your age?" or "There's nothing that we can do for you," invites the patient to seek alternative therapies. Expressions of concern, understanding, and a willingness to help the patient cope with chronic disease respects and serves to meet the medical and psychological needs of the elderly patient. Explanations need to be made in a manner consistent with the sensory and cognitive abilities of the patient and may need to involve caregivers. Other health care team members may be needed to provide care and support. Referral to such individuals is more appropriate than leaving the patient to shop within the health care marketplace. It is also useful to ask patients about their use of unproven remedies.

The physician who responds to health concerns (of the elderly) with, "What do you expect for your age?" or, "There's nothing that we can do for you" invites the patient to seek alternate therapies.

Health care quackery is an important issue in geriatric care. The cumulative burden of disease, the tendency to self-treat, and the high risk of adverse reactions makes quackery of special concern for the doctor who provides care for the older patient.

References

- ¹ Pepper Claude: Quackery: The Need for Federal, State, and Local Response. *The Skeptical Inquirer* 1987;12:70-74.
- ² Soldo BJ, Manton KG. Demography: Characteristics & Implications of an Aging Population. *Geriatric Medicine*, Little, Brown & Co 1988:12-22.
- ³ Besdine RW: Clinical Approach to the Elderly Patient. *Geriatric Medicine*, Little, Brown & Co 1988:23-26.
- ⁴ Coons SJ, Hendricks J, Sheahan SL: A Look at Self-Medication with Non-prescription drugs. *Journal of the American Society on Aging* 1988;12(4):22-26.
- ⁵ Cornacchia HJ, Barrett S: Consumer Health: A Guide to Intelligent Decision. CV Mosby Company 1980:17.

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Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage, although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it, however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

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Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

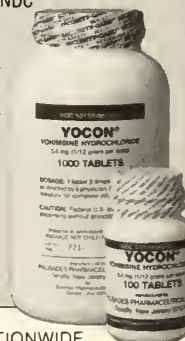
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon[®] 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Pathways and Porches: A Focus on Corridors in Nursing Homes

Renee Rose Shield, PhD

... practical innovations will help transform nursing home environments from dreary, hospital-like settings to places where elderly individuals are respected, appreciated and supported in a sensitive and caring way.

Nursing homes are becoming "home" to increasing numbers of people in our demographically top-heavy state of Rhode Island. The unprecedented rise in the old-old population (those over 85) swells our nursing home population even though it comprises now only 5 percent of people over 65. While we work to provide better medical care for those who are institutionalized, it is also necessary to make the physical environment of nursing homes more suited to the total needs of the elderly.

Nursing homes should become more liveable and more "home-like" as they ensure good caregiving and safety. Strategies for enhancing competence and independence in nursing home residents emerge from knowledge about sensory decline¹ and advances in environmental geron-

tology.² Coupling good environmental design with excellent health care can yield innovative interventions to maintain comfort, identity, and independence among the elderly. In the spirit of the cost-cutting atmosphere we breathe today, environmental design may even make economic sense as it supports the frail elderly person to be as independent as possible, fosters a more pleasurable working environment for staff, and encourages visitors to participate in nursing home life.

For a year a group of architects, physicians, social scientists, nurses, social workers, and designers convened regularly at The Jewish Home to discuss physical improvements in the state's nursing homes. The Design Group focused on four aspects of the nursing home: Corridors, Semi-Public Spaces (such as dining rooms and entrance foyers), Restraints (and their alternatives), and Private Spaces (resident rooms). Our goal was to identify design problems and recommend low-cost, practical solutions to them. This paper presents the suggestions of the Corridor sub-group.

The Nursing Home

The nursing home occupies a special position in society: a low-tech quasi-medical facility that accommodates the disabilities of the residents in as home-like a setting as possible. It must provide both home and hospital functions for its inhabitants. But because the nursing home is not a real home nor is it a genuine hospital, a home-hospital split in the definition of the nursing home creates a tension in function and purpose that can be problematic.³

For example, the typical nursing home usually accommodates the hospital-like functions of the facility, while home-like considerations tend to be secondary afterthoughts (or, often luxurious touches inappropriately designed for this population). These efficient, medical-like environments should not be polarized against a nostalgic reminiscence of past nursing homes, however. Retsinas warns against such romantic simplification:

The homey homes did not offer smoke detectors, sprinkler systems, alarm systems hooked

Renée Rose Shield, PhD, a cultural anthropologist, is clinical assistant professor in the Department of Community Health, Brown University, Providence, Rhode Island.

into local fire stations, fire doors, easy exit points, and nonflammable construction. Benign governmental legislation assaulted nursing homes with a barrage of regulations and specifications and inspections. Investigators, in short, use quasi-hospital criteria to evaluate the nursing home, asking, not how warm a home it is, but how medically sufficient it is.⁵

Design solutions can fulfill . . . mandates without sacrificing the home or hospital imperatives.

Neither extreme of the home-hospital axis is appropriate. The residents' social as well as medical needs are vital; the physical structure must be functional and safe, and it should be appealing to residents, staff, visitors, and inspectors. Design solutions can fulfill these mandates without sacrificing the home or hospital imperatives.

Typical Nursing Home Corridors

Because they are usually modeled on hospitals, many nursing home floors are designed in an H-shape with identical corridors extending from the centrally placed nurses' station, elevator, and dining area. Clash-free neutral colors predominate on walls and linoleum floors. Windows, often placed at the ends of corridors, let in the full sunlight that streams the length of the hall. Handrails line the walls. Notices and ornamental items inform and decorate. Residents' rooms are marked with numbers and printed names. To meet fire and other safety standards, corridors must be of a certain minimal width, be unobstructed, and fulfill numerous specifications for smoke detec-

tors, sprinklers, wall materials, and attachments.^{6,7} To the eye, the corridors stretch long and uninterrupted.

Who Uses Corridors

To assess how the corridors of the nursing home do and should function, we must look at how they are used by three diverse groups of people — the elderly residents, the staff, and the visitors.

The residents: Nursing home residents are very diverse; they range from those somewhat able to care for themselves to those requiring total assistance by staff members. Spanning more than forty years, residents mostly cluster in their 80s and 90s. They have illnesses and disabilities that are multiple, chronic, and individual. Dementing illnesses afflict at least 50 percent of nursing home residents and necessitate varying staff assistance depending upon the severity of the cognitive loss.

Because of resident diversity, the corridors are used in different ways by them. A non-ambulatory resident may be wheeled by his orderly to the outside entrance of his room (when the width of the corridor is wide enough to allow) to watch the comings and goings in the corridor. Others in fragile medical condition are placed in chairs near the nurses' station so that they may be more closely monitored. Ambulatory residents walk unassisted throughout the facility, use the handrails positioned on each wall, or require the assistance of a walker, a cane, or a staff member's arm. Still other residents transport themselves with their wheelchairs. Demented residents often lose their way and may need staff assistance to orient and guide them to their destinations.

The staff: Staff members in a nursing home are varied, too, and include administrators, nurses,

social workers, nursing assistants, orderlies, housekeepers, dietary workers, and other technicians, such as physical and occupational therapists. Physicians are in and out of the institution regularly. The nursing home corridors are also used by ambulance and funeral home personnel as well as state and federal inspectors.

Each staff member's job provides its unique perspective on the corridor. Housekeepers have the daily duty of keeping the corridors sanitary. Durable materials withstand the harsh clean-up of frequent spills, messes, and smells. Dietary staff members use corridors to transport meals and snacks to residents. Nurses wheel medication carts down the corridors regularly. Nursing assistants and orderlies assist residents to and from activities, treatments, dining rooms. Frequent resident room changes, necessitated by changes in level of care, require residents and their belongings to be transported efficiently. Sick and recovering residents must be taken to and from the hospital. For the staff, the corridors are highways for the swift transport of people, equipment, and services.

The visitors: Visitors include residents' families and friends as well as community volunteers. They include children as well as elderly people. Visitors provide companionship to residents by sitting and walking with them in corridors and in their rooms. For visitors the corridors should be appealing, easy to decipher and traverse, and clean. A bland and institutional-looking nursing home may seem dreary, if not forbidding. The efficient and clean look of a typical corridor translates into an impersonal one from the perspective of many visitors, and often creates an emotional obstacle to entering. Visitors want

to find their way with ease and are often misled by identical-looking corridors. Comfortable, semi-private places to socialize with the residents and each other in and around corridor areas help visitors feel at home. The consideration paid to these visitor concerns also reassures them that the individuality of the residents is an important principle of care in the facility.

Sensory Deficits in the Elderly

Sensory impairments present the elderly with numerous difficulties in negotiating the physical world. The quality and extent of these sensory changes vary from individual to individual.¹ The visual and auditory factors that are pertinent to an environmental understanding of the nursing home corridors are briefly outlined here.

Vision: The elderly eye needs three times the illumination necessary for a young person, and, to be effective, lighting should be uniform. Fluorescent lights create flicker which is uncomfortable. Glare to the elderly is blinding and contributes to accidents.¹ Color contrast becomes a necessary aid to elderly as violets, blues, and greens fade out of the color spectrum, leaving reds, oranges, and yellows as the most easily discernible colors.⁸

The elderly eye needs three times the illumination necessary for a young person.

Hearing: "A decline in the ability to hear affects more elderly people than any other chronic condition."¹ In institutional settings auditory loss is particularly augmented by background noise such as vacuum cleaners and loudspeakers. Canned music and frequent interruptions from the corridor loudspeakers interfere with the ability to hear and com-

municate. Even the loud volume of televisions in residents' rooms can disorient those in the corridors.⁹

Principles for Improving Corridor Design

The members of the Corridor group inspected sample nursing home corridors to evaluate their function, safety, and general appeal. We consulted the environmental geriatric literature for pertinent design principles^{2, 10, 11} and we elicited the views of various residents, family members, and staff members. Principles that we consider important for nursing home corridors are the following:

Maintenance. Corridors must be hygienic and durable. The cost of materials must be compatible with the financial realities of health care.

Safety. There should be no obstacles in the corridors. Glare should be avoided; uniform illumination is important to prevent accidents. Handrails should be easy to grasp, and resting places should be available along the way. Staff members need easy visual access to the goings-on of the floor.

Transportation. Corridors should allow efficient transportation of equipment, food, and people, whether this transportation is carried out by staff, residents, or visitors. Staff must be able to reach needy residents quickly. Though appealing in a homey way, carpeting is difficult for residents in wheelchairs or for those using walkers.

Orientation. Corridors should be easily decipherable. Cognitively intact residents as well as visitors need reliable and prominent cues to distinguish identical-looking corridors and floors. Simple and consistent visual signals at decision-points in corridor intersections are helpful. Disoriented residents, profoundly

handicapped in way-finding, are helped by redundant environmental cues to find their destinations more independently.

Socialization and privacy. As transitional spaces leading from here to there, corridors border the private resident rooms, yet are not as fully accessible as such shared spaces as dining room or auditorium. Each corridor is thus a "unit edge," or "critical transition zone where resident and outside world catch glimpses of one another."¹¹ Visual reminders that resident rooms are private homes are necessary. The doorways are important as transition markers. As much as corridors are used for transportation — pathways — they are also employed for sitting, watching, and visiting — porches. Residents, visitors, and staff members should be able to observe activities without being directly involved, be seen by others, and visit with one another with varying amounts of privacy.

Control. The design of corridors can enhance or diminish the individual resident's sense of control over the environment. Distinctive colors or names for corridors help residents, visitors, and staff distinguish among them. The resident who reaches his or her destination aided by redundant environmental cues such as stripes, signs, sounds, activities, and smells, retains the self-esteem of independence. A resident who is encouraged to individualize his doorway or have a variety of seating options in the corridor retains a certain control that is normally precluded in the nursing home setting.

Personalization. Maintaining identity in the institution is vital for nursing home residents and is intimately related to control. Elderly persons, like the rest of us, invest their residences with powerful subjective meanings,¹² and being able to provide continuity

between residences is important. There are easy, low-cost ways to personalize a resident's door or doorway so that it is unique. One has only to look at college dormitory doors for inspiration. A demented resident has an easier time finding his room when the door displays items of which he may be fond or familiar. The restless wandering behavior, so typical of Alzheimer's victims, may be considered an anxious search for familiarity and reassurance. Environmental aids that indicate to the resident that he is "home" may help settle the resident.^{13, 14, 15}

Recommendations

The specific recommendations of the Corridor Group were chosen because they should increase resident comfort, independence, and individuality while they maintain and/or improve function and safety. We are further guided by the principles that the nursing home corridor should be efficient and functional, provide orientation assistance to residents and visitors, be a transitional space between public and private areas in the nursing home, and should allow for varied socialization opportunities. Most of the following recommendations are simple to institute and of low-cost.

- Assess the shininess of wax on floors. The shiny wax is slightly more durable, but it creates glare and may appear slippery to the residents. The main barrier to implementing this recommendation may be cultural bias that shine equals "clean" to inspectors. Teaching them that shine may also equal "falls" may help change this attitude.

- Avoid carpets because they are difficult for walkers and wheelchairs. Furthermore, the noise of vacuum cleaners interferes with routine medical examination and normal conversation.

- Assess the use of the loudspeakers in the nursing home. Reduce loudspeaker interruptions that interfere with resident conversation and social interaction. Avoid canned music.

- Increase electrical outlets in corridors so that electrical cord length of cleaning appliances is reduced. Long cords in the halls are an obstacle for walkers and wheelchairs.

- Paint each corridor with a stripe of a different color. An additional wall stripe from dining area to bathroom orients confused residents. The bright stripe also helps distinguish the wall from the floor.

- Matching the color of a corridor to the color of a resident's wristband helps staff, visitors, and resident find a disoriented resident's room.

- Naming individual corridors helps visitors and residents find their way among identical-looking hallways. Corridors could be named after important people that the residents wish to remember. Suggestions for names can come from home towns, familiar streets, favorite travel destinations.

- Corridors should have uniform, diffused illumination. Fluorescent lights should be lined with low-cost inserts that eliminate the flickering that the elderly find uncomfortable.

- Investigate new, durable, easy to clean wall coverings with pleasing textures. They may be competitive in cost, and they absorb noise.

- Resident doors should be easily discernable and identifiable. The long corridor should be visually interrupted by the rhythm of such doorway markers. Breaking up the long line reduces the institutional corridor to human size. Ideas: doors may be of different colors, archways can be painted around each door, or color tile in the floor linoleum

around the door threshold can indicate the doorway.

Resident doors should be easily discernable and identifiable.

- Patchwork floor tile in the corridor should be avoided. The different colors of the tile suggest changes in levels that can precipitate falls if the nursing home resident adjusts his gait to accommodate this mistakenly perceived step.

- Floors and walls should contrast in color. This feature helps residents distinguish them from each other as well as provide visual interest. Reds, yellows, and oranges should be favored over violets, blues, and greens.

- Bright, large-lettered signs with identifying symbols of a room's function should be displayed prominently on hallways for orientation. The sign for the dining room can be a large place setting, for example. Every redundant orientation cue helps demented residents, promotes independence, and frees valuable time for staff members.

- Resident doorways can be individualized in imaginative ways, should residents desire. A bulletin board can be decorated with what the resident desires to display to others. Such projects can be created in recreational therapy and can involve families and friends, as well as staff. These displays can depict the varied past lives of the residents, create opportunities for conversation and reminiscence, and remind the forgetful or demoralized resident of past achievements, happy events, and current loved ones.

- Wider areas in corridors can be exploited for attractive resident seating and resting, rather than used as parking lots for non-ambulatory or restrained resi-

dents. Semi-circular chair placement creates an inviting inducement for socializing and/or observation. Elevator areas allow residents to see who comes and goes.

- Evaluate corridors in relation to the obstacles that must be overcome by the nursing home residents. Avoid storing unused wheelchairs and other equipment in them. Eliminate laundry bins, linen carts, and cleaning utensils from the corridors whenever possible.

- Depending on the number of confused residents on a particular floor, it may be possible to install a table or shelf around a seating area for the provision of accessible snacks for residents and their visitors.

- Nurses' stations should be central but not seem walled-off to residents and visitors. Low partitions increase the sense of staff accessibility while marking the borders of the nurses' station at the same time.

- Sitting rooms adjacent to corridors should be visually inviting with comfortable, moveable furniture which allows flexible seating arrangements for privacy and socialization. Lighting fixture switches and door knobs should be easy to operate with arthritic hands.

- Walls can be decorated imaginatively. Paintings, resident news, durable tactile wall sculptures, and interesting bulletin board landmarks create interest and decrease the institutional look of the facility.¹⁰

- Visual access to the special function rooms that abut upon corridors, such as physical therapy, can be achieved with a window, creating interest for the staff member, resident, and visitor. Privacy is accomplished through curtains or other window treatment operated from inside the room. Windows with ledges are

opportunities for varied visual display. Overall, windows provide a feeling of openness without complete access.

Resident doorways can be individualized in imaginative ways, should residents desire. A bulletin board can be decorated with what the resident desires to display to others. Such projects can be created in recreational therapy and can involve families, friends, as well as staff.

- Round door knobs should be replaced with levers whenever possible.

- Staff members can be encouraged to wear brighter clothing and institutional uniforms avoided.

- The addition of plants in wide areas of the corridor as well as the nurses' station is another way of adding visual interest, thus breaking up the monotony of a long hallway. Residents may wish to provide the care for the plants, as well. The therapeutic benefit of this activity for nursing home residents has long been noted.^{16, 17, 18} Plants are also likely to enhance a good feeling for staff members and visitors, as well.

Conclusion

Simple and practical recommendations for improving the function and appeal of corridors in nursing home settings also reinforce a sense of home. Such measures help residents to maintain an interest in their surroundings and increase their ability to operate within them. Environmental principles can be utilized to great advantage as a partner in health care for the elderly.

Corridors in nursing homes must be seen from the various

perspectives of those who use them. As health care providers we should remember that the corridors function not only as highways for swift transport of goods, services, and people, but also as pathways for the aged. Finally, corridors serve as porches where residents, visitors and staff socialize and observe the passing scene. From these perspectives it is possible and practical to modify institutional corridors. The recommendations contained in this paper are offered as a means of enhancing independence and self-esteem among residents, while conveying to visitors and staff that individuals are valued, and creating in the process a brighter and more interesting place to live, socialize, visit, and work. These practical innovations will help transform nursing home environments from dreary, hospital-like settings to places where elderly individuals are respected, appreciated and supported in a sensitive and caring way.

Acknowledgments

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References

- ¹ Kalymin Mary. Relationships between Sensory Decline among the Elderly and the Physical Environment: Implications for Health Care. Rhode Island Medical Journal 72(5),161-167,1989.
- ² Lawton MP. Environment and Aging. California: Wadsworth, Inc. 1980.
- ³ Kahana E. A congruence model of person-environment interaction. In PG Windley, TO Byerts, & FG Ernst (Eds.), Theory Development in Environment and Aging. Washington, DC: Gerontological Society. 1975.
- ⁴ Shield Renée Rose. Uneasy Endings: Daily Life in an American Nursing Home. Ithaca: Cornell University Press 1988.
- ⁵ Retsinas Joan. It's OK, Mom: The Nursing Home from a Sociological Perspective. New York: Tiresias Press 1986.
- ⁶ National Fire Protection Association (NFPA). Standard #101. Life Safety Code. 1988.
- ⁷ Minimum Requirements of Construction and Equipment for Hospital and Medical Facilities. Chapter 8 (Long Term Care Facilities). DHEW 1979.
- ⁸ Potter Patricia A and Anne G Perry. Fundamentals of Nursing: Concepts, Process, and Practice. Princeton: CV Mosby Co. 1985.
- ⁹ McHutchion, Edan and Janice M Morse. Releasing Restraints: A Nursing Dilemma. J Gerontological Nursing 15 (2):16-21 1989.
- ¹⁰ Calkins Margaret P. Design for Dementia: Planning Environments for the Elderly and the Confused. National Health Publishing 1988.
- ¹¹ Zeisel John, Gayle Epp, and Stephen Demos. Low Rise Housing for Older People: Behavioral Criteria for Design. Washington, DC: US Department of Housing and Urban Development 1977.
- ¹² Rubinstein Robert L. The Home Environments of Older People: A Description of the Psychosocial Processes Linking Person to Place. Journal of Gerontology: Social Sciences 44:S45-53 1989.
- ¹³ Hall Geri, M Virginia Kirchling and Susan Todd. Sheltered Freedom: An Alzheimer's Unit in an ICF. Geriatric Nursing: 132-137 May-June 1986.
- ¹⁴ Rader Joanne. A Comprehensive Staff Approach to Problem Wandering. Gerontologist. 27(6):756-760 1987.
- ¹⁵ Cleary T Anne, Cheryll Clamon, Marjorie Price and Gail Shullaw. A Reduced Stimulation Unit: Effects on Patients with Alzheimer's Disease and Related Disorders. Gerontologist 28(4):511-514 1988.
- ¹⁶ Avorn J and EJ Langer. Induced Disability in Nursing Home Patients: A Controlled Trial. JAGS 30:397-400 1982.
- ¹⁷ Rowe John W and Robert L Kahn. Human Aging: Usual and Successful. Science 237:143-149 1987.
- ¹⁸ Rodin Judith. Aging and Health: Effects of the Sense of Control. Science 233:1271-1276 1986.

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UNDERSTANDING CME

Edited by
Kimberly Allyn,
RIMS CME Coordinator

Janice Miller, M.Ed.,
Director,
Office of CME
Brown University

The accreditation process for continuing medical education programs may be an unknown area to a number of physicians and other health professionals. Words and phrases such as "accreditation," "the seven essentials," "Category 1 & 2," "ACCME" are often just that — words and phrases. This column is being introduced in an attempt to answer some of the many questions that surface within the CME arena. It is intended to serve as a useful resource to all who are involved in continuing medical education.

Continuing medical education consists of educational activities which serve to maintain, develop or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients, the public or the profession.¹

Rhode Island, as in other states, requires physicians to submit evidence of a minimum of 20 continuing medical education Category 1 hours per year in order to be eligible for relicensure through the Board of Medical Licensure and Discipline.

Category 1 CME activities can only be offered by accredited sponsors of Continuing Medical Education. Rhode Island Medical Society is recognized by the Accreditation Council for Continuing Medical Education (ACCME)

as an accreditor of intrastate continuing medical education programs. RIMS itself does not sponsor individual CME activities for credit. The Brown University Program in Medicine is accredited by ACCME to sponsor continuing medical education for physicians. The Brown CME office gives approval to individual Category 1 CME activities for local, regional, national, or international audiences. Brown does not accredit the CME programs of institutions or organizations.

The purpose of accreditation is to assure physicians and the public that CME activities meet accepted standards of education.¹ Organizations seeking accreditation must document their capacity to conduct educational activities for physicians in a medical or medically related field.

Before the formation of ACCME, the Liaison Committee for Continuing Medical Education (LCCME) was responsible for accreditation activities during 1977-1979. Prior to that, accreditation was under the purview of the AMA's Council on Medical Education. The ACCME is composed of seven organizations:

American Board of Medical Specialties
American Hospital Association
American Medical Association
Association for Hospital Medical Education
Association of American Medical Colleges
Council of Medical Specialty Societies
Federation of State Medical Boards

Evaluation of CME programs is based on the seven Essentials: standards and criteria for accreditation established by ACCME in 1984. The Essentials identify elements of structure, organization and method which contribute to the development of continuing medical education.

ESSENTIAL #1

The sponsor shall have a written statement of its continuing medical education mission, formally approved by its governing body.

ESSENTIAL #2

The sponsor shall have established procedures for identifying and analyzing continuing medical education needs and interests of prospective participants.

ESSENTIAL #3

The sponsor shall have explicit objectives for each CME activity.

ESSENTIAL #4

The sponsor shall design and implement educational activities consistent in content and method with the stated objectives.

ESSENTIAL #5

The sponsor shall evaluate the effectiveness of its overall continuing medical education program and component activities

and use this information in its CME planning.

ESSENTIAL #6

The sponsor shall provide evidence that management procedures and other necessary resources are available and effectively used to fulfill its continuing medical education mission.

ESSENTIAL #7

The sponsor shall accept responsibility that the essentials are met by educational activities which it jointly sponsors with non-accredited entities.

The following definitions will also be useful in gaining an understanding of the accreditation process:¹

CME Accreditation: This is the recognition accorded eligible institutions and organizations which meet the Essentials.

CME Activity: A coherent educational offering which is based upon defined needs, and explicit objectives, educational content, and methods.

A Sponsor: An institution or organization assuming responsibility for CME.

A Participant: A physician engaged in CME.

The Essentials: The document which provides information regarding accreditation and the standards which must substantially be met for a sponsor of CME to be accredited.

Program of CME: The overall CME program of a sponsor consists of one or more educational activities consistent with the Essentials. Accreditation is granted on the basis of the sponsor's dem-

onstrated ability to plan and implement CME activities in accordance with the Essentials. The sponsor's overall program may include occasional CME activities, that do not fully meet the standards for needs assessment, well-defined objectives, curricular design, and evaluation. These activities are part of the accredited sponsor's overall CME program as long as the Sponsor exercises responsibility for these activities through its recognized CME administration unit. The organization should identify those CME activities within its overall program which meet the Essentials.

Designation of CME credit relates to the requirements of credentialing agencies, certificate programs, or membership qualifications of various societies, and the accredited sponsor is responsible to these agencies, programs, and societies in the matter of designation of credits and verifications of physician attendance. The designation of credit for specific CME activities is not within the purview of ACCME or the state medical associations as accrediting bodies.

References

¹ Essentials & Guidelines for accreditation of sponsors of continuing medical education.

Coming Next Month:

What is Category 1 & Category 2?
Explanation of Essential #1 & Essential #2

Questions are encouraged and may be addressed to:

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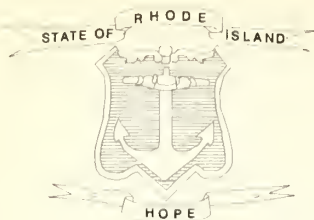
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Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

Rhode Island's Progress in Smoking Reduction

The Centers for Disease Control (CDC) have estimated that the costs of health care and lost productivity due to cigarette smoking amounted to \$284 per person in Rhode Island in 1985, higher than for any other state. This corresponds to total costs statewide of \$273 million for a single year. In another CDC report, Rhode Island ranked ninth among the states in combined mortality (age-adjusted) for chronic diseases, many of which are smoking-related. Rhode Island's rankings in these two studies reflect the historically high rate of cigarette smoking among the state's residents.

Smoking rates in the state have decreased from an estimated 45 percent in 1965 to approximately 27 percent last year, or by about three-quarters of a percentage point per year (Figure 1). If smoking continues to decrease at the same rate for the next decade, the state will fall short of the national Year 2000 Objective for smoking, which is for a smoking prevalence rate of 15 percent. In order to reach this objective, the annual decrease must exceed one percentage point per year. In recent years, smoking among males has decreased at close to the required pace, but among females, the rate of decrease has been much smaller (Figure 2).

Achieving the necessary rate of decrease will be difficult. Simply continuing the current trend will require augmented anti-smoking efforts statewide because many of the remaining smokers are heavier, more addicted smokers. Furthermore, the rate at which young adults began smoking remains higher than is needed in order to help meet the objective (Figure 3). The situation among young females is especially unpromising.

One group in the state has exhibited such a rate of decrease in cigarette smoking over a sustained period. From 1963 to 1988, the smoking prevalence rate among licensed physicians has decreased by 1.1 percentage points per year.

In order to achieve this rate of decrease, physicians have demonstrated some remarkable changes in smoking behavior. As of 1988, seven out of eight physicians who had ever smoked no longer did so, and less than 3 percent of the youngest physicians smoked. These figures are in stark contrast to those for the general population.

Physicians can play an instrumental part in reducing the impact of smoking in Rhode Island. Having achieved a virtually smoke-free profession, the challenge is now to convince their patients of the merits of quitting smoking or of never starting. Counseling by physicians is an effective incentive for many smokers to quit and can contribute substantially to Rhode Island's progress toward the Year 2000 Objective for smoking.

Data Sources

1965: Estimated from the National Health Interview Survey.

1975-1985: Rhode Island Health Interview Survey.

1986-1989: Behavioral Risk Factor Surveillance System.

Physicians: Rhode Island Physician Smoking Surveys.

References

Centers for Disease Control. Chronic Disease Reports: Deaths from Nine Chronic Diseases — United States, 1986. *Morbidity and Mortality Weekly Report* 36:17-20 (January 19, 1990).

Centers for Disease Control. Smoking and Health. A National Status Report (2nd Edition). Rockville, Maryland: Department of Health and Human Services, Office on Smoking and Health. Publication No. (CDC) 87-8396 (revised February 1990).

Figure 1. Smoking Prevalence Rate and Projected Rate by Year, Rhode Island, 1965-2000

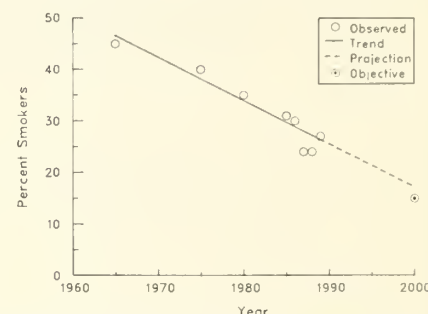


Figure 2. Smoking Prevalence Rate by Sex, Rhode Island, 1965-1989

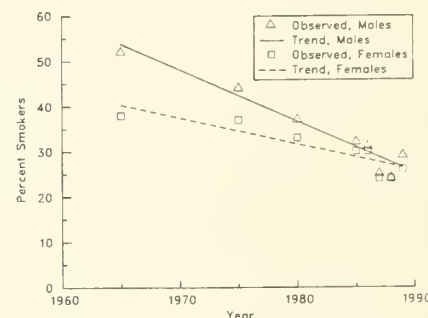
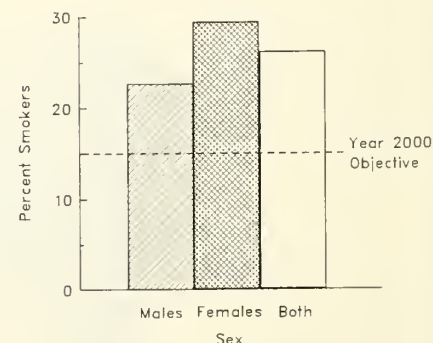


Figure 3. Average Smoking Prevalence Rate for Persons Ages 18-24, by Sex, Rhode Island, 1985-1989



Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period December 1989	12 Months Ending with December 1989	
	Number	Number	Rates
Live Births	1,282	15,295	15.4*
Deaths	902	9,726	9.8*
Infant deaths	(13)	(157)	10.3†
Neonatal deaths	(10)	(121)	7.9†
Marriages	478	8,272	8.3*
Divorces	309	3,639	3.7*
Induced Terminations	671	7,827	511.7†
Spontaneous Fetal Deaths	62	1,121	73.3†
Under 20 weeks' gestation	(53)	(1,004)	65.6†
20+ weeks' gestation	(9)	(106)	6.9†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period September 1989	12 Months Ending with September 1989		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	236	3,450	347.4	4,459.5
Malignant Neoplasms	195	2,451	246.8	7,474.0
Cerebrovascular Diseases	41	604	60.8	1,033.0
Injuries (Accident, Suicide, Homicide)	40	418	42.1	9,732.5
COPD	15	288	29.0	401.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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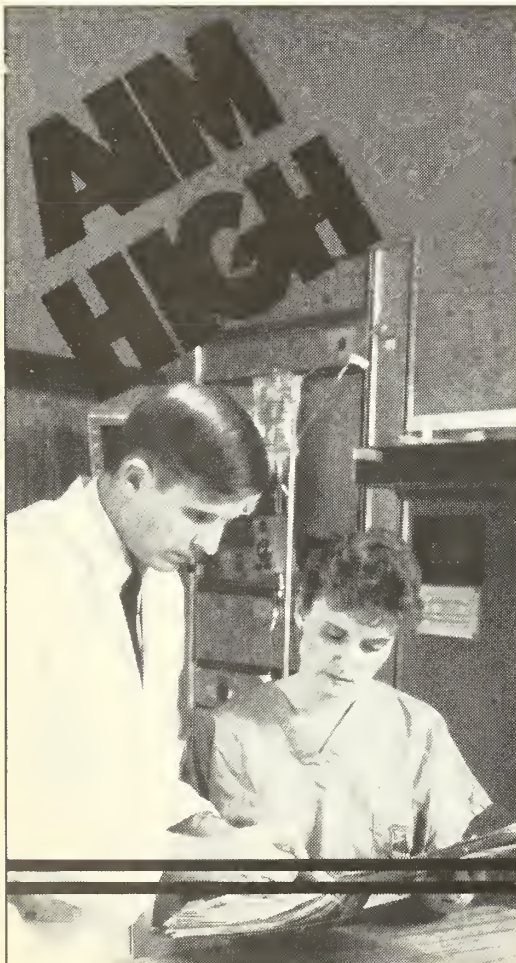
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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (April, 1940)

The first article in this issue of the *Journal* represents an address given by C. Holmes Boyd at the Interne Alumni Clinic Day of Memorial Hospital, Pawtucket, on the subject of the association between bacterial endocarditis and syphilitic heart disease. The author notes at the beginning that the engrafting of a bacterial endocarditis upon a syphilitic valve "... has in general been considered a rarity."

The paper then summarizes eleven previously reported instances of bacterial endocarditis superimposed upon a syphilitic valvulitis and adds six further cases which he has abstracted from the autopsy records of the Baltimore City Hospital. Among 8,100 post mortem protocols, he found 105 cases of pathologically verified bacterial endocarditis, and of these 105, fourteen "... were felt definitely to be satisfactory examples of vegetative bacterial endocarditis superimposed of old syphilitic valve disease." However, adequate tissue for further microscopic study was available in only six of these eleven cases, and these six instances form the basis of this report.

Five of the six cases were admitted in marked cardiac failure and the sixth with lobar pneumonia. During their clinical

course, all showed "... fever of a septic type with peaks from 102.5 to 104 degrees. Chills were not a feature in any case." Four of the six cases demonstrate significant anemia on admission.

Of the six new cases, five are male, and the ages range from 30 to 44 years. In none is there any history suggesting rheumatic fever. Serology (Wasserman test) is positive in four, and in the remaining two, there is a satisfactory history of antiluetic therapy.

The author concludes: "Clinical diagnosis of the association of bacterial endocarditis with syphilitic valvular disease is at best difficult, but should be suspected in any case of supposed syphilitic aortic insufficiency which runs a continuous febrile and downhill course, especially if any of the usually associated signs, such as progressive anemia, etc., are present. However, definite diagnosis can be made only after careful anatomical study, not only for positive features, but to rule out other conditions which might produce the primary valvular change."

Dr Samuel Morein of Providence presents a paper on the medical management of gastric and duodenal ulcer. He bases his therapeutic recommendations upon his personal experience with 650 cases of duodenal ulcer and 57 patients with gastric ulcer.

The author's summary states:

"Gastric and duodenal ulcer are primarily chronic recurrent medical disease entities of civilized man prone to occur in individuals of dynamic or hyperemotional character. During their life cycle, complications may arise when surgical intervention may be necessary. Good results may be obtained under adequate medical management in the large majority of cases. In only a small number of patients may surgical intervention be an absolute indication as an adjunct to management; these indications are definite and are: perforation, true cicatricial pyloric obstruction, repeated massive hemorrhages endangering the life of the patient, intractable ulceration or a suspicion of gastric malignancy. A valuable procedure in the management of pyloric obstruction and of intractable cases of peptic ulcer is described. People should be warned that attacks of recurrent indigestion, no matter how mild they may be, should not be treated lightly. They should seek competent medical advice without any undue delay. True cooperation and genuine teamwork between the surgeon and internist is absolutely essential as in diabetes and pulmonary tuberculosis. A person harboring an ulcer must be thoroughly convinced to treat his ulcer with respect and not abuse it with alcohol and tobacco; by overeating, or by the

ingestion of indigestible food or irritating drugs, and above all, to avoid emotional upsets and physical strain. Finally, in order to treat a peptic ulcer as successfully as possible, the physician must treat his patient's ulcer as if it were his own, remembering that the life cycle of ulcer in an ulcer bearing individual, ends only with the life of the individual."

The principal editorial recommends that the local hospitals adopt a patient-record filing system based upon consecutive discharge numbers. A subsequent editorial notes that the post-office has issued a two-cent stamp with a likeness of Dr Crawford W. Long, the Georgian physician who, on March 30, 1842 had given ether for a surgical operation. The editorial observes further the important contributions of Connecticut's Dr Horace Wells in using nitrous oxide for a dental extraction in 1844; Massachusetts' Drs Charles Jackson and William Morton in using ether for surgical insensibility in 1846; and Edinburgh's James Simpson, in 1847, in using chloroform for obstetrical purposes. Finally, the editorial notes that the word, anesthesia, was coined by Dr Oliver Wendell Holmes in 1846.

* * *

Twenty-Five Years Ago (April, 1965)

The principal paper is entitled, Regional Hypothermia, I — Effectiveness in Renal Vascular Occlusion in the Dog, and is written by Drs Shu H. Yoon and Ernest K. Landsteiner from the Department of Urology of the Rhode Island Hospital.

Because temporary interruption of the renal blood supply is increasingly necessary in surgery

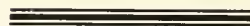
of the kidney, the authors undertake a study to determine renal tolerance to experimental anoxia. The kidneys of dogs are studied at varying intervals following the clamping of their renal arteries under normothermic and hypothermic conditions.

The authors conclude: "(1) With the kidney at normal temperature, clamping of the renal artery for periods less than 30 minutes produces little or no parenchymal damage to the kidney of the dog. However, clamping for longer periods consistently produces moderate to severe renal damage. (2) The optimal period of time during which cooling (with a saline-filled plastic bag at 2° to 4° C.) need be applied to the kidney is approximately 10 minutes in the dog. (3) Renal hypothermia is produced most rapidly if the renal artery is clamped during the period of cooling. (4) The technique of producing local hypothermia is more effective if the renal artery alone, rather than both artery and vein, is occluded. (5) Regional hypothermia definitely affords protection against parenchymal deterioration from interruption of blood supply to the kidney. In fact, in the case of the dog at least, the period during which the kidney may be clamped without residual damage is extended from 30 minutes to at least one hour and perhaps more."

A case report of idiopathic jaundice of pregnancy is presented by Dr D.R. Baronian. The author notes that "... The condition is striking in that it occurs in the last trimester of pregnancy, clears up completely after delivery, and frequently occurs in a high percentage of cases during subsequent pregnancies." He states further: "It is important that this disorder be differentiated from extrahepatic jaundice due to gallstones, so that unnecessary surgery be avoided."

Drs A.G. Czekanski and O.F. Smith report the first published case in Rhode Island of small bowel ulceration due to thiazide tablets containing enteric coated potassium.

An editorial discusses a newly discovered byproduct of the paper pulp industry, dimethyl sulfoxide (DMSO), and notes that early observations hint of miraculous capabilities. It is said to "kill pain, speed wound healing, reduce inflammation, clear up bruises, relieve certain pollen and bacteria caused allergies, relax muscles, hasten excretion of poisons from the body, and relieve some types of arthritis and bursitis."



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References

1. *USP DI Update*, September/October 1988, p 120.
2. *Br J Clin Pharmacol* 1985;20: 710-713.
3. Data on file, Lilly Research Laboratories.
4. *Scand J Gastroenterol* 1987;22(suppl 136): 61-70.
5. *Am J Gastroenterol* 1989;84: 769-774.

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3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

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Carcinogenesis, Mutagenesis, Impairment of Fertility—A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

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an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect, but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

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Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumentary—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage—Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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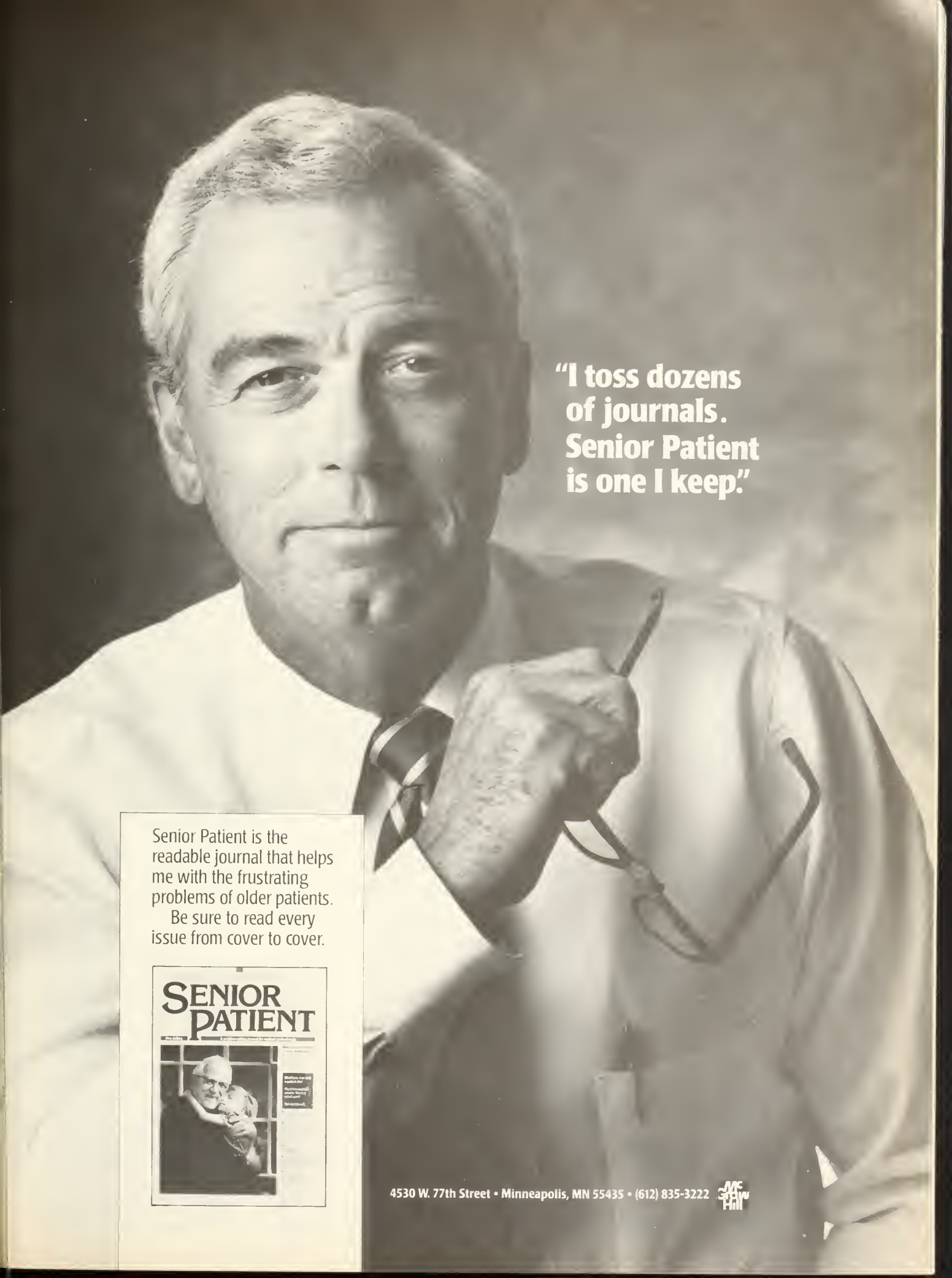
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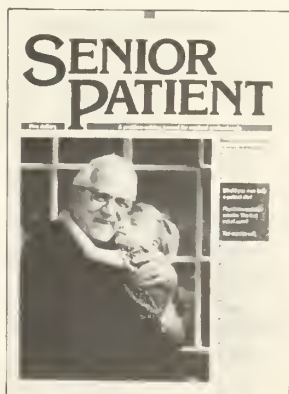
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PHYSICIANS IN THE NEWS

Recent appointments at Memorial Hospital include **Dr Steven B. Kirschner** to the Department of Medicine's Division of Gastroenterology and **Dr Mark A. Robbin** to the gastroenterology staff.

* * *

New officers to the Medical Staff of Landmark Medical Center include **Dr David B. Stoll**, President; **Dr Francis L. Scarpaci**, Vice President; **Dr Andrew Ruthberg**, Secretary/Treasurer; and **Dr Edward P. Andersen**, Past President. Department chairmen include **Dr Paul C. Hessler**, Chairman, Department of Radiology; **Dr Jan J. Penkala**, Chair-

man, Department of Obstetrics and Gynecology; **Dr Daniel Halpren-Ruder**, Chairman, Department of Emergency Medicine; **Dr E. James Monti, Jr**, Chairman, Department of Pediatrics; **Dr Naeem Siddiqi**, Chairman, Department of Surgery; and **Dr Tilak Verma**, Chairman, Department of Medicine.

* * *

Dr Martin Keller has been appointed professor and chairman of psychiatry and human behavior at the Brown Medical School. He will serve as executive psychiatrist-in-chief at Butler Hospital, Bradley Hospital, Rhode Is-

land Hospital, Roger Williams General Hospital, Miriam Hospital and the Veterans Administration Medical Center.

* * *

The Board of Trustees and Administrative staff at Newport Hospital presented **Dr Charles A. Hall, Jr**, internist, with the Medical Staff Member of the Year award. **Dr Paul C. Houston**, surgeon, was selected as Physician of the Year. These awards were presented at a Medical Staff recognition dinner to honor the active members of Newport Hospital's medical staff.

CME CALENDAR

Title: Improve Your Reimbursement Thru Proven Solutions to Medicolegal Challenges

Sponsored by: Medical Society of the State of New York

Date: April 25-26, 1990

Location: University Club, West 54th Street, New York, New York

Objective: Professionals attending the conference will learn newly developed methods of communicating medical information.

For more information: Jemi Goodman, (516)742-6100

Presented by: Medical Risk Management Advisory Corp.

* * *

Title: Ambulatory Surgery '90

Focus on Excellence
16th Annual Meeting

Date: May 2-5, 1990

Location: Anaheim, CA

Program: Includes a variety of topics all oriented to quality care

in the ambulatory surgical facility.

For more information: Federated Ambulatory Surgery Association, Alexandria, VA
(703)836-8808

* * *

Title: Rural Health!

Empowered To Make A Difference

Sponsored by: National Rural Health Association

Date: May 16-19, 1990

Location: New Orleans, LA

Objective: Provides rural health professionals with the educational and networking opportunities to be empowered to achieve success in rural health care.

For more information:

National Rural Health Association
301 E. Armour Blvd. Suite 420
Kansas City, MO 64111

Title: AIDS & ETHICS

Sponsored by: Bioethics Consultation Group, Inc., Berkeley, CA
International Institute of Bioethics, Luxembourg

Kaiser Permanente Medical Care Program, Oakland, CA

Park Ridge Center for the Study of Health, Faith & Ethics, Chicago, IL

The Healthcare Forum, San Francisco, CA

Date: June 24-27, 1990

Location: San Francisco, CA

Purpose: To create a forum where health care providers, policy specialists, persons living with HIV infection or AIDS, community-based organization managers, and government officials can explore the values conflicts behind many AIDS policy and treatment questions.

For more information: Krebs Convention Management Services, (415)255-1297

The AMA Hospital Medical Staff Section Fifteenth Assembly Meeting June 21-25, 1990 Chicago Marriott Hotel Chicago, Illinois

Highlights of the Annual Meeting will include:

- an educational program entitled, "Building Effective Hospital Physician Relationships: Ten Success Stories"; Stephen M. Shortell, Ph.D. will present the results of his study on the working relationships between ten selected hospitals and their medical staffs;
- presentation by the AMA-HMSS Governing Council of reports on medical staff issues including the Impact of Hospital Bankruptcy, the Role of Hospital Governing Boards in Professional Review, and Information Sharing Among Medical Staffs;
- recommendation of policy to the House of Delegates on Prioritization of Health Care Expenditures and Notification of Denials by the PRO;
- AMA-HMSS Governing Council elections for the positions of Chairman, Vice-Chairman, Secretary, and one Member-at-large.

For Information Contact:

Department of Hospital Medical Staff Services
American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610
Phone (312) 645-4754 or 645-4761



HMSS

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Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal*.

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½ × 11 inch firm typewritten paper, double-spaced throughout (including title page, text, acknowledgments, and references) with margins of at least one inch and using but one side of each page. Tables, charts, and legends should be submitted separately from the text, and referred to by number (ie, Fig. 1) within the text. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title Page: All manuscripts must include a title page which provides the following information: (1) a concise and informative title; (2) the name of the author or authors with their highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointment, and primary hospital affiliation; (4) mailing address and office telephone of principal author; (5) mailing address of author responsible for correspondence or reprint requests; (6) source of support if applicable.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white 5×7 glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in the text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten on a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be appropriately masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive numbers of illustrations. Color plates are not acceptable.

Identification of Patients: Names, initials should not be used. Use of numbers is a preferable form of identification.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

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References: To conserve space and expense, references should be limited to those essential to the subject. The editor reserves the right to reduce the number when it is deemed necessary. The references must be double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

Correspondence: All correspondence relating to publication should be addressed to: Managing Editor, *Rhode Island Medical Journal*, 106 Francis Street, Providence, RI 02903.



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Warnings: *Angioedema:* Angioedema of the face, extremities, lips, tongue, glottis, and/or larynx has been reported in patients treated with ACE inhibitors, including VASOTEC. In such cases, VASOTEC should be promptly discontinued and the patient carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL), should be promptly administered.** (See ADVERSE REACTIONS.)

Hypotension: Excessive hypotension is rare in uncomplicated hypertensive patients treated with VASOTEC alone. Patients with heart failure given VASOTEC commonly have some reduction in blood pressure, especially with the first dose, but discontinuation of therapy for continuing symptomatic hypotension usually is not necessary when dosing instructions are followed; caution should be observed when initiating therapy. (See DOSAGE AND ADMINISTRATION.) Patients at risk for excessive hypotension, sometimes associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death, include those with the following conditions or characteristics: heart failure, hypotension, high-dose diuretic therapy, recent intensive diuresis or increase in diuretic dose, renal dialysis, or severe volume and/or salt depletion of any etiology. It may be advisable to eliminate the diuretic (except in patients with heart failure), reduce the diuretic dose, or increase salt intake cautiously before initiating therapy with VASOTEC in patients at risk for excessive hypotension who are able to tolerate such adjustments. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients at risk for excessive hypotension, therapy should be started under very close medical supervision and such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart disease or cardiovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of VASOTEC, which usually can be given without difficulty once the blood pressure has stabilized. If symptomatic hypotension develops, a dose reduction or discontinuation of VASOTEC or concomitant diuretic may be necessary.

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: *General Impaired Renal Function:* As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta-adrenergic-blocking agents, methylglucoside, nifedipine, calcium-channeling agents, hydralazine, prazosin, and digoxin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radioactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not

been clearly defined, VASOTEC[®] (Enalapril Maleate, MSO) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome. Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypotension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of ¹⁴C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2967 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were: headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were: dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were: fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), angina pectoris (1.5%), nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring since the drug was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients (see WARNINGS, Hypotension); pulmonary embolism and infarction, pulmonary edema, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis (hepatoacutal or cholestatic jaundice), melena, anorexia, dyspepsia, constipation, glossitis, stomatitis, dry mouth.

Musculoskeletal: Muscle cramps.

Nervous/psychiatric: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Respiratory: Bronchospasm, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, anosmia, tinnitus, conjunctivitis, dry eyes, hearing.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgias/arthritis, myalgias, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 11% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g/dL and 1.0 vol %, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: *Hypertension:* In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed. If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium (see PRECAUTIONS).

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance > 30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 2.5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure and hypotension, the maximum daily dose is 10 mg. If the patient's serum creatinine is > 1.6 mg/dL, therapy should be initiated at 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d., then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more, if at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function. The maximum daily dose is 40 mg.

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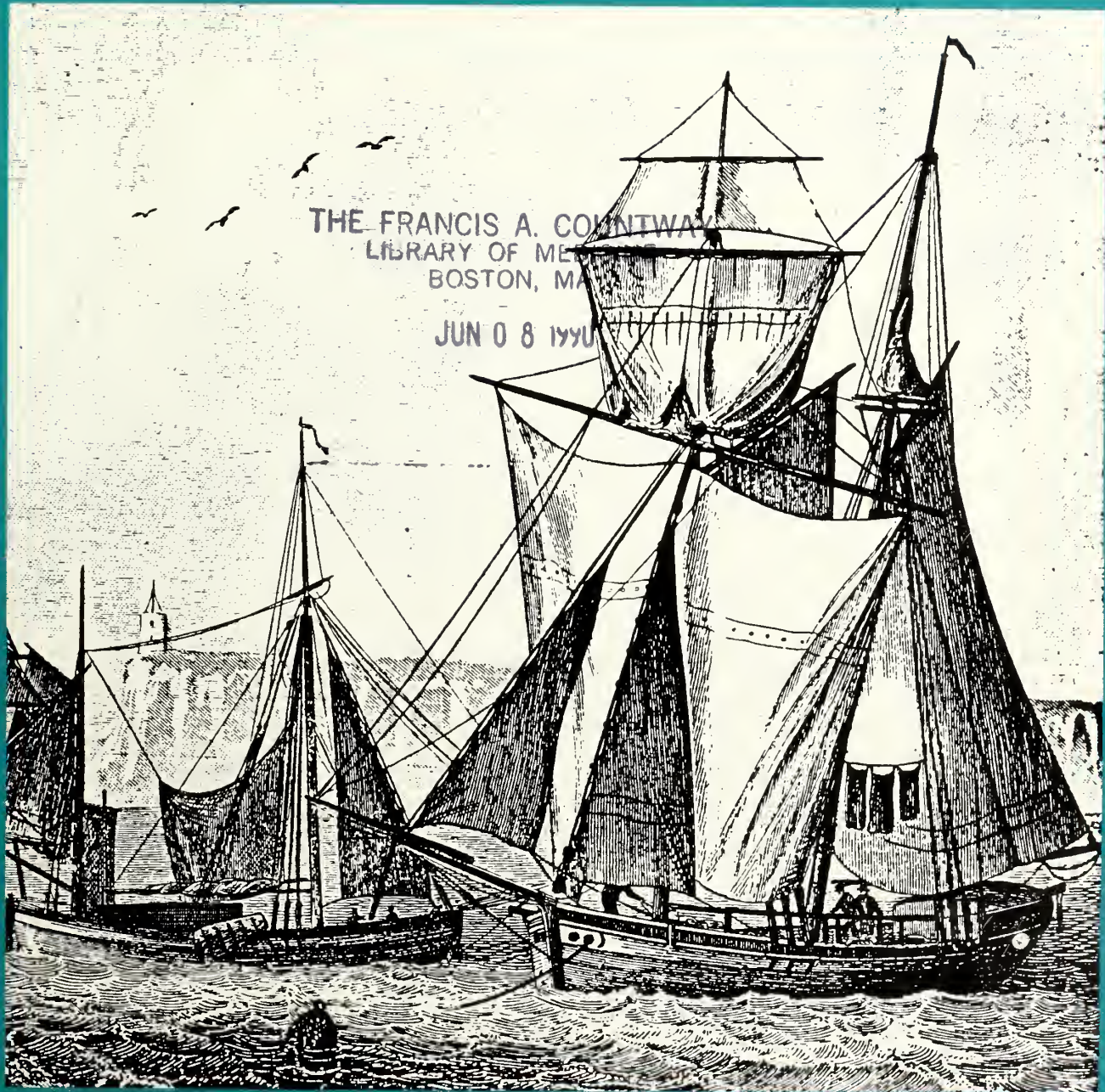


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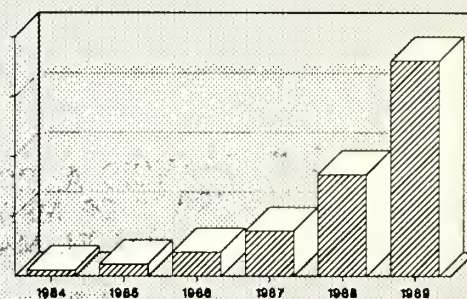


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EDITORIALS

International Health in Rhode Island

Years after I had chosen my present career, I overheard my grandmother complaining to my parents, "Why couldn't he specialize in something I could get?" This comment only underscores the problem of relevance that plagues tropical disease specialists in the United States. Two decades ago, over half of the United States medical schools didn't include tropical disease in their core curriculum. Even today, the in-depth study of "exotic" diseases is relegated generally to a few schools of public health. With the recent explosion in international travel, particularly to the Third World, as well as the many new Americans arriving in Rhode Island, illnesses that had been considered "zebras" are now relatively commonplace in this state. Since my arrival in Providence four years ago, I have treated numerous cases of malaria and typhoid fever as well as a wide variety of parasitic infections including amebic liver abscess, cysticercosis, schistosomiasis, clonorchiasis and filariasis.

For many years Dr Alfred Senft was the only tropical disease specialist at Brown University's medical school. In the private sector, Rhode Island had always had a few physicians who were familiar with these diseases, generally through their past service in the military. In 1985, Dr Steven Opal came to Brown and opened Rhode Island's first Traveler's Clinic at Memorial Hospital in Pawtucket (401-722-6000, ext.

2545). I arrived in the following year to start a new International Health Program at Brown and began Miriam Hospital's Traveler's Clinic (401-274-3700 or 331-8500, ext. 4075). In 1988, the State Health Department relinquished its responsibilities for travel immunizations to these two clinics which now function as the sole source of both official information and vaccinations with the State. Currently, the International Health Institute at Brown has seven tropical disease specialists who are involved in research (both in Rhode Island and overseas), teaching and patient care.

The purpose of this issue of the *Rhode Island Medical Journal* is to acquaint Rhode Island physicians with some of the current problems in tropical medicine relevant to their practices. In retrospect, my grandmother was wrong; there are many international health problems that Rhode Islanders can get, and we as physicians need to be prepared to deal with them effectively.

G. Richard Olds, MD
Guest Editor

The Importing of Fevers

Exotic diseases with lengthy names and multicellular agents with even lengthier names made up much of the fabric of those medical school courses variously called parasitology or tropical

disease. Prior to World War II these arcane, "foreign" illnesses were taken seriously only by the rare medical student considering a career in either public health or missionary medicine. Certainly an enduring familiarity with schistosomiasis or malaria or cholera was considered unnecessary for the practice of temperate climate medicine.

But then came American military encounters with such unfamiliar places as Guadalcanal, Saipan, Burma, Bizerte, Iwo Jima, Pusan and Saigon. And following these wars came the numerically greater civilian movements, voluntary and involuntary, in the form of a two-way stream of tourists seeking recreation, and refugees looking for sanctuary in the United States. With increasing mobility both of persons and pathogens, tropical diseases no longer restricted themselves to the tropics. Medical school study of the illnesses of hot, steamy, far-off places now assumed greater immediacy.

The Centers for Disease Control (CDC), the United States Public Health Service institution for the recording of reportable illness, now provides surveillance statistics of certain communicable disorders within the United States. Through its informative publication *Morbidity and Mortality Weekly Report*, the incidence rates of such infections as amebiasis, anthrax, brucellosis, cholera, arthropod-borne encephalitis, leprosy, malaria,

plague, trichinosis, typhoid and typhus are routinely reported. It is instructive to see how the events making up our nation's recent history have impinged upon the secular trends of these communicable diseases.

In the case of malaria, for example, there was a moderate rise in its incidence rate, within the United States, following World War II, reaching about 65 cases per 100,000 population per year, and accounted for largely by returning veterans. In the succeeding five years the rate dropped to about 2/100,000. Malarial relapses affecting Korean War veterans then caused the rate to climb to about 5/100,000. By 1965, however, the rate had fallen to 0.07/100,000, its lowest level thus far. At the height of the Viet Nam conflict the rate rose again to 1.1/100,000, falling by 1974 only to rise again because of immigrant civilians with malaria, largely from Southeast Asia, Mexico, Nigeria and Borneo.

During the first six weeks of 1990, the CDC has reported 106 new cases of malaria in residents of the United States.

Malarial transmission *within* the United States, in contrast to the importation of active cases, is unusual. Since 1950, 21 discrete outbreaks of indigenous malaria, all caused by *Plasmodium vivax*, have been reported, most occurring in the southern counties of California. In one such incident, in San Diego County, a cluster of 30 persons (largely migrant agricultural workers) developed acute, clinical malaria between July and September of 1988. All denied prior malaria, intravenous drug abuse or blood transfusions. The two necessary components to provide an explanation for these cases (namely, a local index case of malaria and a competent insect vector) were both documented. A worker with ma-

laria had recently moved into the community and numerous *Anopheles hermi* mosquitoes were subsequently trapped in the vicinity.

This issue of the *Journal*, edited by Dr G. Richard Olds, is devoted to a consideration of the medical hazards which the civilian tourist may encounter when travelling, and some prudent steps that he or she may undertake to lessen these risks.

Stanley M. Aronson, MD

Cholera Comes to Providence, 1832

Before 1817, cholera was a disease known only to those familiar with the Ganges delta of eastern India. In August of 1817, cholera left its epidemic home in Bengal to spread west through India as an accompaniment of various religious migrations and British army campaigns. By 1820 it had infiltrated all of India, affecting about seven percent of its population. It then spread east to the Philippines, Borneo and the Celebes; and west to Asia Minor and the Middle East. By 1823 it reached the Caspian Sea to involve the Russian city of Astrakhan, its first landfall in Europe. All of continental Europe was involved by 1831 and the first case of cholera in England was recorded in the North Sea port of Sunderland on November 4, 1831.

On June 1, 1832, cases of cholera appeared in the newly arrived immigrant populations of Quebec. The disease spread rapidly throughout Lower Canada and shortly emerged in the northern border communities of Vermont and New York. On Friday, July 27, 1832, two cases of cholera were reported in Newport and on Thursday morning, August 2,

1832, four cases of cholera (three adults and one child) were recognized in the Eddy Street waterfront district. The epidemic in Providence would not subside until the early weeks of winter.

In 1832, Moses Brown helped to supervise a small Quaker school, then called the Yearly Meeting School, and located on the east side of Providence. On July 7, 1832, in response to the imminence of epidemic cholera, Moses Brown and Hannah Gould prudently closed their school and dispatched the following circular to the parents of the dismissed children:

Esteemed Friend:

The subcommittee of the Boarding School under the advisement of the meeting for Sufferings have come to the conclusion, in consequence of the existence of the Spasmodic Cholera in various places which have frequent communication with this city, thus rendering it probable that we may be visited by this fatal malady, that it will be most prudent to discontinue the School for a season. We therefore request thee to cause the removal of thy child or children from the School as soon as practicable.

The Sub-Committee have come to this conclusion from a sense of their duty to the Institution, to the children and to their parents, apprehending that in all cases of such threatening danger, it would be the desire of parents to have their children under their immediate care. Information will be given thee when the committee deems it proper again to open the School, which we hope will be at no distant day. On behalf and by appointment of the Committee.

Moses Brown Hannah Gould

The *Journal* thanks Mr David Burnham, Headmaster of Moses Brown School, for sharing this document which was derived from the historic archives of his institution, and is reproduced on the following page.

Stanley M. Aronson, MD

County of Essex, Vermont, Providence, N. H. Nov. 7th 1832.

Esteemed Friends: The sub-committee of the Boarding School under the patronage of the meeting for sufferings have considered the constitution, in consequence of the distance of the Massachusetts Charities in various places which have frequent communication with this city, thus rendering it probable that we may be misled in this fatal mistake, that it will be most prudent to discontinue the school for a season - We therefore request those to cause the removal of the child or children as soon as practicable.

The Committee have come to this conclusion from a sense of their duty to the Institution, to the children and to their parents, apprehending that in all cases of ^{such} threatening danger, it would be the desire of parents to have their children under their immediate care. Information will be given thee when the Committee deem it proper again to open the school, which we hope will be at no distant date.

On behalf & by appointment of the Committee

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Travel to Developing Countries: Pre-Departure Medical Advice

Rodrigo L. Romulo, MD
Peter M. Wiest, MD
Steven M. Opal, MD
G. Richard Olds, MD

It has . . . become important for physicians in Rhode Island to be more familiar with the prevention and management of the more common of these (tropical) diseases.

Over ten million Americans travel to developing countries each year.¹⁻³ They will frequently be exposed to diseases with which they and their physicians are unfamiliar. At the Traveler's Clinics of the

Rodrigo L. Romulo, MD, is a Fellow in Geographic Medicine at The Miriam Hospital, Providence, Rhode Island.

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Steven M. Opal, MD, is Assistant Professor of Medicine at Brown University and Director of The Traveler's Clinic, Memorial Hospital, Pawtucket, Rhode Island.

G. Richard Olds, MD, is Associate Professor of Medicine and Director of the International Health Institute at Brown University, Providence, Rhode Island.

Miriam and Memorial Hospitals, over four thousand travelers sought pre-travel advice as of June, 1989. The great majority of these traveled to Africa, Asia and South and Central America, areas where many exotic tropical diseases are endemic. It has therefore become important for physicians in Rhode Island to be more familiar with the prevention and management of the more common of these diseases. It is the purpose of this article to familiarize Rhode Island physicians with some of the preventive aspects of travel medicine, primarily general advice about travel, immunizations, prophylactic medications, and presumptive treatments of common travel-related illnesses. (Management of the sick returning traveler with fever, diarrhea or eosinophilia will be discussed in other articles in this issue of the *Journal*.)

General guidelines for travelers are available in "Health Information for International Travel," published and updated yearly by the Centers for Disease Control (CDC). Specific recommendations must be adjusted to specific

locations within a country, as well as to the duration and type of travel anticipated. Current information should always be obtained from travelers clinics, local health departments or the CDC as legal requirements and medically indicated precautions abroad are subject to sudden change.

General Recommendations

An individualized program to maximize each traveler's health when abroad requires detailed

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

CDC: Centers for Disease Control

DEET: N, N diethylmetatoluamide

DNA: Desoxyribo-nucleic acid

HDCV: Human diploid cell vaccine

HIV: Human Immunodeficiency Virus

ID: Intradermal

IG: Immune globulin

IM: Intramuscular

IPV: Inactivated polio vaccine

OPV: Oral polio vaccine

knowledge of the duration and nature of the trip, the traveler's exact itinerary, age, medical, allergy and immunization history. Emphasis must be given to proper eating and drinking habits since the majority of travel-related health problems occur through the ingestion of contaminated food or drink.

Pre-travel consultation should include a discussion about common problems related to international travel including jet lag, high altitude sickness, environmental exposures, the hazards of insects such as vectors for multiple infections (malaria, yellow fever, dengue, filariasis, trypanosomiasis, onchocerciasis, etc.) and the means to avoid these vectors. Travelers to remote areas must be warned about venomous animals, rabies, and the hazards of fresh water swimming (schistosomiasis, leptospirosis, non-cholera vibrios) as well as how to deal with a medical emergency.

There is also increasing concern about the acquired immunodeficiency syndrome on the part of both travelers and host countries.¹⁷⁻¹⁸ Although it is the opinion of the World Health Organization that the small benefits of screening travelers would not justify the diversion of resources from educational programs and measures to protect blood supplies, some countries, such as the People's Republic of China, are now requiring HIV testing for travelers applying for more than a two month visa. Known HIV-positive individuals who wish to travel abroad are therefore likely to be subject to increasing restrictions. Of concern to all travelers is the risk of exposure to contaminated blood or nonsterile needles that might be used in an emergency. HIV infection is an issue throughout the third world but the greatest risk presently is for travel to

Central and East Africa where HIV infection is at least as common as in the United States.

Immunizations for Travel:

General Guidelines

Immunization is only one aspect of a comprehensive disease prevention program for travelers. Since no vaccine is completely safe and effective, risks and benefits for each particular traveler must be evaluated prior to their use. Only immune globulin (IG) has been shown to be highly cost-effective when given as passive protection against Hepatitis A.⁴

Pre-travel consultation should include a discussion about common problems . . . including jet lag, high altitude sickness, environmental exposures, the hazards of insect vectors. . . and the means to avoid these vectors.

Confusion exists regarding immunizations that are required by law and those that are recommended for medical reasons. Only two vaccines, yellow fever and cholera, are required by law for international travel. Some vaccines are recommended to adults whether or not they are traveling and must be updated prior to travel (diphtheria/tetanus, measles, polio). Other immunizations are recommended because travelers may acquire a particular disease in a country or in a specific location within that country (typhoid, meningococcal meningitis, rabies, hepatitis B, and Japanese B encephalitis).

In general a traveler should allow four to six weeks before departure for optimal vaccine administration since some vaccines require more than one dose for full protection while some

vaccines are incompatible with others. Theoretically, one live virus vaccine may interfere with the antibody response of a second live virus vaccine given within one month of the first. Also, immune globulin (IG) may interfere with the antibody response to live attenuated virus vaccines. Ideally, IG should not be given for three months before or at least three weeks after most live virus vaccines. It is, therefore, recommended that live virus vaccines be administered during the first pre-travel visit and that IG be given later, as close to departure date as possible. Inactivated vaccines, in general, can be given simultaneously although local and systemic reactions make this undesirable.

Vaccines produced in eggs are contraindicated in persons with known hypersensitivity reactions to eggs. Potential recipients of these vaccines should be questioned about any prior adverse reaction resulting from eating eggs. Live virus vaccines should not be given to pregnant women or those likely to become pregnant within three months of immunization. Live viral vaccines should also be avoided in immunocompromised individuals (eg, those with lymphoreticular and generalized malignancies, acquired immunodeficiency syndrome, or those receiving corticosteroids, alkylating agents or radiation therapy).

Required Immunizations

Yellow fever: Yellow fever is a mosquito-borne viral illness similar to other hemorrhagic fevers but with more severe hepatic involvement. It exists only in Africa and South America. Yellow fever vaccine is a live, attenuated virus vaccine developed in chick embryos that is safe and effective. It consists of a single shot that must be renewed in ten years. It is rec-

ommended for all persons six months of age or older, traveling to areas in Africa or South America. Yellow fever vaccination is required by law by some countries (not the United States) for travelers arriving from an endemic area.⁵ It should be given at least two weeks prior to travel to be effective. Concomitant or prior immune globulin administration may inactivate the vaccine and reduce antibody response as may administration of cholera vaccine within three weeks of the yellow fever vaccine. Yellow fever vaccine is given only in state-licensed centers because it requires cold storage and is viable for only a short time after reconstitution. In Rhode Island, the only state-licensed vaccination centers are the Traveler's Clinics at the Memorial and Miriam Hospitals.

Cholera: Cholera is an acute non-inflammatory diarrheal illness caused by *Vibrio cholera* O-group 1 obtained by ingesting contaminated food or water. The risk to US travelers is thought to be exceedingly low.⁶ The cholera vaccine is a killed bacterial vaccine consisting of two shots given at least one week apart for the primary series and requiring single booster shots after six months. It is of limited effectiveness. The World Health Organization has attempted to have this vaccination removed from the list of required immunizations by all countries. It is our practice to administer only a single dose to meet the legal requirement for travel between certain countries, particularly in Africa and Asia. The complete primary series is recommended only for those who live and work in endemic areas under less than adequate sanitary conditions or those with compromised gastric defense mechanisms (antacid or H2-blocker ther-

apy, achlorhydria, gastrectomy). Although this vaccine can be obtained by any Rhode Island physician, it is probably inappropriate to administer the vaccine if the official "stamp" cannot be provided to the traveler.

Only two vaccines, yellow fever and cholera, are required by law for international travel.

Smallpox: Smallpox vaccination should not be required by law by any country but on occasion certain countries may require travelers to have this vaccination. Since this vaccine is not available to civilians in the United States and may even be dangerous, a letter stating that the smallpox vaccination has not been given "for medical reasons" is sufficient to allow transit in these rare circumstances.

Universally Recommended Immunizations

Diphtheria-tetanus: Tetanus and diphtheria remain problems worldwide and adults should be immunized with the combined diphtheria-tetanus (bacterial toxoid) vaccine.⁷ A booster within the last five years eliminates the need for additional tetanus immunization (with a potentially non-sterile needle) or tetanus immune globulin if the traveler sustains a penetrating wound overseas.

Measles: Measles in the United States has continued to decline but a large percentage of cases is being imported.⁸ Most persons born in the United States before 1956 are likely to have been naturally infected but with decreasing exposure to natural cases of measles in the US during the last two decades, unvaccinated persons may reach adulthood still susceptible. Other susceptible

persons include those who were given live measles vaccine before fifteen months of age and those who received inactivated (killed) vaccine. Recipients of the latter vaccine (available in the US from 1963-1967) when exposed to natural virus are at risk of developing the atypical measles syndrome which can be severe and occasionally with serious complications. These susceptible groups of people, together with those born after 1956 with no documented record of immunization, should receive a single dose of live attenuated virus vaccine.

Polio: Poliomyelitis remains a major medical problem worldwide with over 250,000 cases reported in 1986.⁹ Travelers to countries where the risk of exposure to wild polio virus is increased should be fully immunized. There are two vaccines available for poliomyelitis. Trivalent oral polio vaccine (OPV) is a live viral vaccine and is the immunization of choice for infants, children and adolescents up to eighteen years old unless contraindicated.

For adult travelers who were previously unvaccinated or whose immunization status is unknown, primary immunization with inactivated polio vaccine (IPV) should be given. This is because there is a slight (one in three million) risk of vaccine-associated poliomyelitis in adults receiving OPV for the first time. IPV should be boosted every five years for international travel. Rare cases of paralytic polio have been reported in immunocompromised recipients and close contacts of OPV-vaccinated persons. IPV should therefore also be used for such individuals.¹⁰

Other Recommended Immunizations

Other immunizations are recom-

mended because travelers may acquire the disease in a particular country or in a specific location within that country. These include immune globulin, typhoid, meningococcal meningitis, rabies, hepatitis B, and Japanese B encephalitis vaccines.¹¹⁻¹⁴

Immune Globulin: Most travelers from industrialized nations are susceptible to hepatitis A, which is the most frequent, serious illness in travelers. The virus is transmitted through fecally contaminated food and water. Published attack rates vary from 1/150 to 1/500 for a routine two-week trip to most developing countries. Travelers to such countries can decrease their exposure to hepatitis A by avoiding contaminated food or water and especially avoiding shellfish.

Immune globulin (IG) has been shown to be highly effective in preventing hepatitis A and may also provide some protection against hepatitis B and non-A, non-B hepatitis. For adults, 2 cc of IG is given intramuscularly for trips of two months duration or less, while 5 cc is of benefit for up to four to six months. Ideally, IG should not be given with or prior to immunizations with live attenuated virus vaccines.

Unfounded concerns have been raised by travelers concerning potential HIV transmission through the use of IG.¹⁵ HIV antibodies were transiently measured after administration of the older immune globulin preparations prior to HIV screening of donor blood. These individuals were never infected with the virus. No case of AIDS or even HIV seroconversion has ever been associated with IG administration. Present lots of immune globulin are free of detectable HIV by culture or DNA hybridization techniques. Even if the virus were to inadvertently enter the pool it

would be inactivated during the preparation of IG. Given the demonstrated safety of immune globulin and the serious nature of hepatitis A infection, passive immunization should be encouraged in all travelers to developing countries. It is in fact our practice to routinely administer this injection to ourselves and our families prior to travel abroad.

Typhoid: *Salmonella typhi*, the etiologic agent of typhoid fever, is transmitted by fecally contaminated food and water and is prevalent in Africa, Asia and Central and South America. Hundreds of thousands of cases are reported worldwide each year.¹⁶ The estimated attack rate for American tourists is about 1/10,000 to 1/50,000.

Travelers to endemic areas if previously unvaccinated should be given typhoid vaccine for prolonged (more than three weeks) travel, as should persons with increased risk of infection (achlorhydria, immunosuppressed, sickle cell anemia). The typhoid vaccine is a killed bacterial vaccine which consists of a primary series of two shots at least a month apart. If there is insufficient time for the two shot series in a previously unvaccinated traveler, an accelerated schedule of three shots one week apart may be used. This may not, however, confer as much protection as the standard two-shot series. A single booster is given to previously immunized persons if three or more years have elapsed since the primary series. It should be emphasized that all travelers, including typhoid vaccine recipients, must still be cautious in selecting food or water since the protective effect of the vaccine may be overcome by an increased inoculum. Side effects of this vaccine are common (fever, chills, pain at injection site). It is therefore advan-

tageous to complete this series well in advance of travel.

Meningococcal Meningitis: Several areas of the world including Northern India, Nepal, sub-Saharan Africa and Saudi Arabia have epidemics of meningococcal meningitis.¹¹ Most travelers have a low risk of acquiring meningococcal bacteremia or meningitis but it is difficult to decrease potential exposure since the disease is transmitted by airborne lipid droplets during prolonged contact with the local populace. Such activities as riding in trains and planes with natives puts travelers at risk. Serogroup A is the most common cause of epidemics outside the US, but serogroups B and C have also been associated with epidemics. Vaccination with the quadrivalent A, C, Y, W-135 meningococcal vaccine is recommended for travel to high risk areas. Recently, some countries have even required immunizations of all travelers during an acute outbreak. A booster dose is required every three years.

Rabies: Travelers to rabies endemic areas of the world (Central and South America, Asia, the Middle East and Africa) should be informed about the risks of infection related to contact with domestic and wild animals.¹² Pre-exposure prophylaxis with human diploid cell vaccine (HDCV) is recommended for persons in high risk groups, such as those living in or visiting endemic countries (especially rural areas) for prolonged periods. Since immunization should be initiated within 72 hours of a bite it is also recommended for any traveler who will be more than three days from medical care no matter how short the stay. Those whom we usually immunize include Peace Corps volunteers, missionary families, field biologists, trekkers

in Nepal, and spelunkers who explore caves that may be inhabited by bats.

A pre-exposure series with HDCV consists of three injections, intramuscular (IM) or intradermal (ID), if completed thirty days before travel. ID is half the cost of IM. If less than thirty days is left before departure IM injection is preferred. Also, concomitant use of chloroquine interferes with antibody response induced by ID injection of HDCV. Pre-exposure vaccination also significantly protects the individual if post-exposure therapy cannot be initiated in 72 hours.

Hepatitis B: The prevalence of hepatitis B virus carriers in developing countries is high (up to 20 percent). Hepatitis B vaccination is recommended for those who have direct contact with blood or bodily secretions (physicians, nurses, other health care workers), those traveling for more than six months in highly endemic areas (sub-Saharan Africa, Southeast Asia including China, Korea, South Pacific Islands, the interior Amazon basin, Haiti, Dominican Republic) and those having sexual contact with residents of these areas.

Two hepatitis B vaccines (plasma-derived and recombi-

nant) are available in the United States. The full series consists of three shots, the first two being given a month apart and the third six months after the first. Some protection is provided by one or two doses. The need for booster doses has not been determined. The optimal injection site in adults is in the deltoid muscle.

Japanese B Encephalitis: Japanese B Encephalitis is a mosquito-borne viral encephalitis that occurs in epidemics during rainy months in India, Bangladesh, China, Korea, Laos, Nepal, Burma, Vietnam, the eastern parts of the USSR, and northern Thailand. In endemic areas of Southeast Asia (Indonesia, Southern Thailand, Sri Lanka, Malaysia and the Philippines) the risk is lower and there is no seasonal distribution.¹³ Persons at risk are those living for more than three months in endemic or epidemic areas. A highly effective vaccine is produced by several companies in Japan but is currently not available in the United States. It is hoped that this situation will be corrected soon but until then high-risk travelers may inquire about the availability of the vaccine at American embassies in countries where Japanese B encephalitis is endemic or

epidemic. As with all vaccinations anticipated to be given overseas we routinely prescribe sterile disposable needles with a prescription since we cannot be sure that these materials can be obtained easily. The vaccines themselves are readily available in most developing countries. Most physicians in these countries use reusable (hopefully autoclaved) needles and syringes.

Malaria Prophylaxis

Malaria is transmitted by the bite of the female *Anopheles* mosquito and is the leading parasitic cause of death worldwide. Almost all cases of fatal malaria are associated with *Plasmodium falciparum* and a primary goal of prophylaxis is to prevent infection with this species. The female *Anopheles* mosquito is most active from dusk until dawn and measures to avoid this insect vector including the use of appropriate clothing, netting and insect repellents (>30 percent DEET) are extremely important and must be stressed.

Prophylactic drugs have also been shown to be effective. *P. vivax*, *P. malariae*, and *P. ovale* remain sensitive to chloroquine but many strains of *P. falciparum* are chloroquine-resistant. The need for, and type of, prophylaxis is usually dependent on the exact itinerary within a given country. The itinerary should be thoroughly reviewed and compared to information on areas of risk within a given country. The risk of acquiring chloroquine resistant *P. falciparum* should also be determined. A complete discussion of this topic is contained in the article by Weist, et al, in this issue of the *Journal*.

Traveler's Diarrhea

Traveler's diarrhea refers to an acute illness with sudden onset



of watery diarrhea, cramps, nausea and general malaise. Between 20 to 50 percent of travelers to developing countries will develop diarrhea during or shortly after their trip. The disease is transmitted through fecally contaminated food or water. Travelers to Africa, Latin America, Southeast Asia and India are at highest risk. Although often self-limited, the diarrhea may be serious enough to impact significantly on a traveler's itinerary. For methods of prevention and treatment of traveler's diarrhea please refer to the article by Opal, et al, in this issue of the *Journal*.

Jet Lag

After undergoing sudden changes in time zones, especially after crossing more than three time zones, most travelers experience the symptoms of jet lag.¹⁰ These include fatigue, insomnia, decreased appetite, change in bowel habits and headache. Approaches recommended to deal with jet lag include such common sense measures as eating and sleeping well prior to departure. Recently a special jet lag diet has received attention. This advises a pattern of sleep/wake cycles and a feast-fast-feast-fast diet based on the time in the planned destination. This was shown to decrease symptoms and adjustment time in US military personnel in trans-Atlantic flights. Short acting benzodiazepines such as triazolam (Halcion®) may be helpful in relieving insomnia but we do not recommend the routine use of these drugs.

Dehydration often accompanies prolonged air flights owing to the low relative humidity in aircraft flight cabins. Dehydration will worsen symptoms of jet lag. Fluid volume depletion during air travel can be minimized by drinking liberal quantities of non-carbonated, non-alcoholic beverages.

Caffeinated drinks should be avoided.

Motion Sickness

This may occur with any form of transportation but especially with travel aboard ships. Symptoms include nausea, vomiting, malaise, fatigue, headache, dizziness, and often vertigo. Medications given prior to exposure may be helpful. These include antihistaminics (meclizine, dimenhydrinate, and cyclizine) and anticholinergic agents such as scopolamine. The latter, however, have significant side effects such as dry mouth, blurring of vision, and may precipitate acute angle closure glaucoma, hallucinations, disorientation and urinary retention especially in the elderly. These side effects are less common with transdermal scopolamine especially when used in younger adults. Patches can also be removed if side effects develop and last for up to three days.

High Altitude Sickness

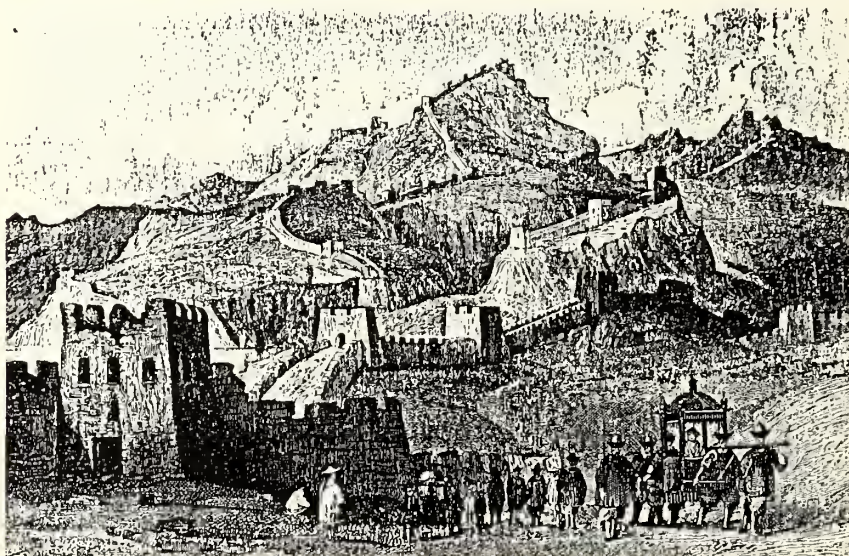
Travelers who make rapid ascents to high altitudes (eg, mountain climbers) may experience any of a spectrum of altitude-induced illnesses including acute mountain sickness (mild to severe headache, lassitude, insomnia or

nausea), high altitude pulmonary edema (severe noncardiac pulmonary edema), and high altitude cerebral edema (symptoms of increased intracranial pressure).¹⁹ Prevention of high altitude sickness by slow ascent of not more than 1000 feet per day is advisable but often impractical for most climbing expeditions. Travelers should be advised to decrease physical activity during the first few days and to avoid alcohol. Oral acetazolamide (Diamox®) and dexamethasone have been shown to decrease or prevent symptoms of acute mountain sickness. In general, however, we do not recommend the use of these medications for regular tourist travel.

Dehydration will worsen symptoms of jet lag. Fluid volume depletion during air travel can be minimized by drinking liberal quantities of non-carbonated, non-alcoholic beverages. Caffeinated drinks should be avoided.

Heat Stroke

Travelers or athletes who exercise vigorously in hot weather



without being acclimatized may experience this most severe of heat-related injuries.²⁰ It is a medical emergency and may also affect elderly patients or those with chronic diseases. Heat-related illness may also be exacerbated by diuretic use. Symptoms include weakness, fatigue, nausea, vomiting or headaches, with mental status changes that may progress rapidly to coma. Mortality can be high and avoidance of such vigorous exercise in hot weather should be practiced. Most heat-related problems can be avoided by the use of proper clothing (light, long-sleeved, loose fitting, cotton clothing, use of a hat) and keeping well hydrated. Powdered "Gatorade" can be reconstituted with water and may be particularly useful.

Summary

Travelers to developing countries are at risk of contracting tropical infectious diseases that they or their physicians may be unfamiliar with. Proper pre-travel counsel should be given concerning general health risks that may be encountered abroad, immunizations, malaria prophylaxis and prevention and treatment of traveler's diarrhea. In Rhode Island, expert advice may be obtained at the Traveler's Clinics at the Miriam Hospital in Providence (401-274-3700 or 331-8500, ext. 4075) and the Memorial Hospital in Pawtucket (401-722-6000, ext. 2545). The Miriam Traveler's Clinic is open Wednesday (9-1) and all day Friday while the Memorial Traveler's Clinic is open Tuesday afternoon. These Traveler's Clinics are headed by Drs G.R. Olds and S.M. Opal, respectively.

Addendum

Three new events have occurred of importance to the readers: The first is that there have been widespread outbreaks of meningococ-

cal meningitis in Kenya and Tanzania. During the last 6 months travelers have periodically been required to show valid immunization with a polyvalent meningococcal meningitis vaccine. It is now the official recommendation of the Centers for Disease Control, and ourselves, that all travelers to this part of the world receive this immunization prior to departure. The second important update concerns measles immunizations. We are all aware of the recent outbreaks of measles on our college campuses and the national problem of increasing cases of measles among children under a year of age. New recommendations from the Centers for Disease Control strongly recommends dual immunization of children at 9 and 13 months and the reimmunization of all young adults born after 1956 prior to international travel. Finally, this Spring, a new four-dose oral typhoid vaccine will become available. This far less toxic and more effective vaccine will be expensive but may change our current indications.

References

- Centers for Disease Control: Health information for international travel. US Department of Health and Human Services Publication No. (CEC) 88-8280, 1988.
- Salata RA, Olds GR: Infectious diseases in travelers and immigrants. In: Tropical and Geographic Medicine. Warren KS, Mahmoud AAF, eds., McGraw-Hill Book Company, New York, NY, 1989.
- Allard R: Problems in adequately immunizing international travelers. *Can Med Assoc J* 128:40-41, 1983.
- Conrad ME, Lemon SM: Prevention of endemic icteric viral hepatitis by administration of immune serum globulin. *J Infect Dis* 156:84-91, 1987.
- Centers for Disease Control. Immunization Practices Advisory Committee: Yellow fever vaccine. *Ann Intern Med* 100:540-542, 1984.
- Centers for Disease Control. Cholera vaccine. *MMWR* 27:173-174, 1978.
- Committee on Immunization: Guide for adult immunization American College of Physicians, Philadelphia, 1985.
- Katz S: Measles — forgotten but not gone. *N Engl J Med* 313:577-578, 1985.
- World Health Organization. Poliomyelitis — the childcrippler. Update No. 6, 1988.

- Jong ES: The travel and tropical medicine manual. Philadelphia, Pennsylvania. W.B. Saunders Company, 1987.
- Leopold ML, Gold R: Meningococcal A and other polysaccharide vaccines. A five year progress report. *N Engl J Med* 308:1158-1160, 1983.
- Fishbein DB, Pacer RE, Holmes DF, et al: Rabies pre-exposure prophylaxis with human diploid cell rabies vaccine: A dose response study. *J Infect Dis* 156:50-55, 1987.
- Denning DW, Kaneko Y: Should travelers to Asia be vaccinated against Japanese B encephalitis? *Lancet* 1:863-864, 1987.
- Steffen R, Richenbach M, Wilhelm V, et al: Health problems after travel to developing countries. *J Infect Dis* 156:84-91, 1987.
- Centers for Disease Control: Safety of therapeutic immune globulin preparations with respect to transmission of Human T-lymphotropic virus type III/lymphadenopathy associated virus infection *MMWR* 35:231-233, 1986.
- Warren JW, Hornick RB: Immunization against typhoid fever. *Ann Rev Med* 30:457-572, 1979.
- Quinn TC, Mann JM, Curran JW, et al: AIDS in Africa: An epidemiologic paradigm. *Science* 234:955-968, 1987.
- World Health Organization. Acquired Immunodeficiency Syndrome (AIDS): consultation on international travel and human immunodeficiency virus (HIV). *WHO Wkly Epidemiol Rec* 62:77-78, 1987.
- Hackett PH, Roach RC, Sutton JR: High altitude medicine. In: Management of Wilderness and Environmental Emergencies. Auerbach PS, Geehr EC, Eds. CV Mosby Company, St. Louis, Missouri, 1989.
- Yarborough BE, Hubbard RW: Heat related illness. In: Management of Wilderness and Environmental Emergencies. Auerbach PS, Geehr EC, Eds. CV Mosby Company, St. Louis, Missouri, 1989.

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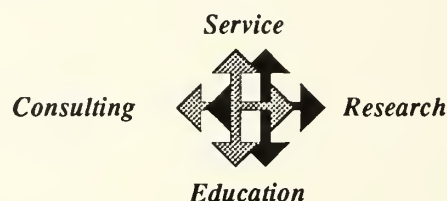
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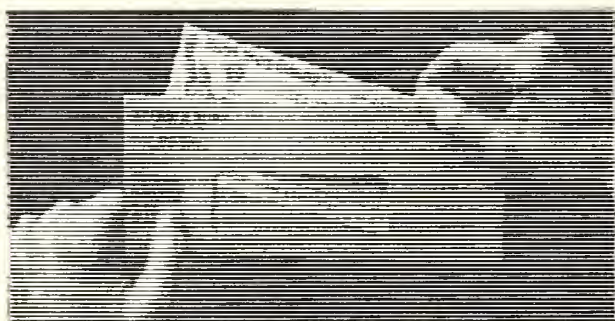
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Eosinophilia in Immigrants and Returning Travelers

Maya Rogers, MD
G. Richard Olds, MD

The number of circulating eosinophils rises in response to immediate hypersensitivity reactions and the invasion of the body by large multicellular helminths.

Case

B.W. was a 21-year-old graduate student who spent six months with the Anthropology Department studying the tribal behavior of the pygmy people in Western and Central Zaire. He took malaria pills while there and returned feeling well. Six months after his return, he developed a swollen, pruritic left wrist. The wrist was erythematous, warm, and markedly swollen involving most of the back of the hand. He was seen by a physician who prescribed antibiotics for cellulitis. The swelling slowly resolved over the next 5-8 days. Similar pruritic swellings developed five times over the next two years, usually

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over the wrists but also the ankles, back and forearms. Each episode was associated with a marked peripheral blood eosinophilia (>2000 eos/mm³). He was seen by several specialists who often diagnosed chronic urticaria or angioedema. Treatment was usually with topical steroid creams and antihistamines. Occasionally he received a course of antibiotics. He was referred to the Traveler's Clinic.

With this clinical presentation, Loa Loa was strongly suspected. A *D. imitus* titer was positive at over a 1:2000 dilution. Microfilaria were not found in day or night specimens but diethylcarbamazine (DEC) treatment evoked a massive inflammatory reaction over the left wrist three days into therapy. Eosinophilia resolved over the subsequent five months. This traveler's case exemplifies classic Loa Loa, the tissue nematode.

* * *

The purpose of this article is to acquaint the Rhode Island physician with the problem of eosinophilia in a recent immigrant or a traveler returning from the trop-

ics. The etiology is frequently a helminth infection but the diagnosis is often missed because the physician caring for the patient fails to elicit the appropriate history, does not check an absolute eosinophil count or is unfamiliar with tropical parasitic infections.

An elevated eosinophil count in a non-traveling native Rhode Islander is uncommon. The differential diagnosis includes allergies, drug reaction, collagen vascular disorders, and malignancies. As in the case described, an elevated eosinophil count in returning travelers suggests a helminth infection¹. Recent immi-

ABBREVIATIONS USED:

CDC: Centers for Disease Control

CT: Computerized tomography

DEC: Diethylcarbamazine

ELISA: Enzyme-linked immunonabsorbent assay

FDA: Food and Drug Administration

IgE: Immunoglobulin E

LFT: Liver Function Tests

O&P: Ova and Parasites

eos/mm³: absolute eos count per cubic millimeter

grants often have eosinophilia: it is present, for example, in 10-50 percent of Southeast Asian immigrants to the United States.²

Eosinophil Structure and Function

The number of circulating eosinophils rises in response to 1) immediate hypersensitivity reactions and 2) the invasion of the body by large multicellular helminths. The regulation and function of the eosinophil has only recently been clarified.³⁻⁵ Eosinophils are probably derived from pluripotential stem cells located in the bone marrow. The eosinophil's maturation is associated with acquisition of crystalloid granules which stain with eosin giving the cell its name. These characteristic eosinophilic granules contain a variety of enzymes such as arylsulfatase and myeloperoxidase as well as major basic protein which assist the cell in its primary function of destruction of extracellular targets including worms.⁶

Eosinophil number, migration and activation are controlled by a variety of polypeptides including eosinophilopoietin derived from T cells, a polypeptide similar in function to erythropoietin for red cell regulation. Eosinophils are primarily tissue-based white cells and are frequently found along the GI tract, in the skin, lung and uterus. These cells are attracted to the appropriate tissue sites of inflammation by a variety of stimuli including complement fragments and lymphokines as well as parasite-derived molecules themselves.⁷ These stimuli also activate the eosinophils and make them more efficient in parasite killing. Complement or antibody mediated degranulation of eosinophils on the surface of invading helminths damages these nonphagocytosable organisms.¹

Helminths

Helminths are multicellular, macroscopic organisms. They differ from many other infectious agents of man in that some stage in their development usually occurs outside the human host and may necessitate parasitization of two or more nonhuman hosts. Humans generally become infected by ingestion of eggs, or by larval penetration through unbroken skin or by the bite of an arthropod vector. Once within the human host, the immature worms migrate to a defined location where they either mature in the tissues (the tissue nematodes, larval cestodes and trematodes) or pass out of the tissues into the more protected environment of the colon (intestinal nematodes and cestodes).

Intestinal Nematodes

The intestinal nematodes are the most common cause of eosinophilia in returning travelers.⁹ They cause eosinophilia only during their migratory phase through tissues. The peripheral eosinophil count will return to normal when these worms reach the intestine and lay eggs, at which time stool for ova and parasites will be positive. Persistent eosinophilia suggests ongoing exposure. Worms that do not invade tissues such as enterobiasis (pin worm) and trichuris trichiura (whip worm) do not cause eosinophilia. Nematodes with migratory phases include *Ascaris*, hookworm and *Strongyloides* as well as animal counterparts of *Ascaris* and Hookworm (Table 1).

Ascaris lumbricoides is a large intestinal round-worm of global distribution. Following ingestion of ascaris eggs in soil, second stage larva penetrate the mucosa of the small intestine and migrate to lung or liver via blood or lymph. The growing larvae then migrate through the upper respiratory tract

TABLE 1. Intestinal Nematodes

<i>Ascaris lumbricoides</i>
Hookworm (2 species)
<i>Strongyloides stercoralis</i>
<i>Toxocara canis</i>
<i>Toxocara cati</i>

and are swallowed a second time where they go on to mature into adults in the small intestine. Egg laying occurs 60-75 days after infection and it is only at this time that stool for ova will be positive.

The intestinal nematodes are the most common cause of eosinophilia in returning travelers. They cause eosinophilia only during their migratory phase through tissues.

Ascaris lumbricoides is a very common parasite infecting up to 80 percent of Africans and over a billion individuals worldwide. Humans commonly become infected because of fecal/oral contamination. Travelers may ingest eggs on food that has been improperly cleaned or prepared, for instance in salads handled by infected chefs who do not wash their hands. Patients may be asymptomatic, have vague to severe abdominal pain or, in rare circumstances, biliary colic associated with obstruction. Cough is associated with transient eosinophilic pulmonary infiltrates. The diagnosis is made through serology and by finding eggs in stool weeks to months after exposure. Since eosinophilia occurs only transiently during the nematode's initial migration, and reinfection is uncommon in travelers after their return, this etiology of eosinophilia generally resolves without specific treatment. However, adult worms then persist for years in the gastrointestinal tract. Treatment with me-

bendazole is usually effective in eradicating infection.

Hookworms (*Ancylostoma duodenale* or *Necator americanus*) are 5-13 mm nematodes that reside in the small intestine. Travelers may become infected by walking barefoot or lying on beaches without towels. This disease is frequently seen in immigrants: worldwide, over a billion people are infected. Larvae penetrate the skin and migrate through the circulation to the lungs and upper respiratory tree. There they penetrate alveolae, migrate up the trachea and are swallowed. In the gastrointestinal tract, the hookworms attach to the intestinal wall, mature and begin laying eggs in 40 to 100 days. Adult worms use host red blood cells for nutritional support. The most frequent disease syndrome produced by these nematodes is iron deficiency anemia usually seen in children with heavy infections secondary to recurrent or massive exposure. "Ground itch" can occur at the site of skin penetration. Transient bronchitis and pneumonitis are uncommon but may occur as the developing helminths migrate through the lungs. Eggs in stool are diagnostic but will not be positive in the early stages of infection at which time serology is useful. Treatment with mebendazole has a 40-60 percent cure rate. Failures are often given a trial of thiabendazole. Ivermectin (currently not approved for this use by the FDA) may eventually be the drug of choice.

Strongyloides stercoralis is an unusual helminth in that, in contrast to almost all other helminths, replication and autoinfection can occur within the human host without reexposure. A study of 178 World War II ex-prisoners of war showed that 33 were still infected 40 years after exposure.¹⁰ This occurs because the strongyloides life cycle allows

for two routes of development: infective filariform larvae can exist and multiply either within man or outside in the soil. Infection of man occurs initially through skin penetration similar to hookworm. Worms migrate to lungs and are swallowed. Prefilariform larvae called rhabditiform larvae appear in stool approximately 3 weeks after exposure. These larvae can repenetrate the lumen of the bowel and cause another infection cycle leading to chronic eosinophilia.

Travelers may become infected (with hookworm) by walking barefoot or lying on beaches without towels. This disease is frequently seen in immigrants: worldwide, over a billion people are infected.

Strongyloides are widely distributed in tropical and subtropical regions. Symptoms and signs of acute infection are generally associated with heavy worm burdens and range from no symptoms to mild or severe abdominal pain. Other nonspecific gastrointestinal complaints such as indigestion and intermittent diarrhea are also seen. Mild, persistent eosinophilia is common. Chronically infected patients who are treated with immunosuppressive agents may develop severe disseminated strongyloidiasis. These patients present with intense abdominal pain, shock, gram-negative bacteremia or pulmonary symptoms associated with massive larval penetration of the bowel and subsequent invasion of the lungs and other tissues. Unfortunately because of the underlying immunosuppression, serum eosinophil counts are generally normal. To diagnose strongyloidiasis multiple fresh stool speci-

mens should be examined but stools may be negative in up to two-thirds of lightly to moderately infected cases. Recently an enzyme-linked immunoabsorbent assay (ELISA test) has been useful in making the diagnosis in these patients.^{11,12} Thiabendazole is used to treat *S. stercoralis* but ivermectin may become the drug of choice in the future.

The round worms *Toxocara canis* and *Toxocara cati* usually parasitize dogs and cats respectively but can cause diseases in humans when embryonated eggs in animal feces are ingested accidentally. Unable to complete their normal life cycle in the human host, these nonhuman ascaris counterparts undergo extensive somatic migration causing the syndrome, visceral larva migrans. A history of pica and exposure to puppies is frequently obtained and patients, especially children, may present with fever, hepatomegaly and eosinophilia. In contrast to the nonhuman ascaris counterpart, the nonhuman hookworm causes cutaneous larva migrans following direct penetration of the skin by larvae. Serpiginous, pruritic eruptions characterize cutaneous larva migrans. Travelers are frequently exposed to these parasites when they walk barefoot on beaches. Because these worms never mature in the human host, eggs are never found in stool and eosinophilia is always present. A positive ELISA test confirms the diagnosis of either condition. Treatment for cutaneous larva migrans is with thiabendazole. There is no proven effective therapy in visceral larva migrans although thiabendazole is frequently used. Steroids are reserved for life-threatening cases.

Tissue Nematodes

Tissue nematodes are the second most common cause of eosino-

philia in returning travelers.⁹ These roundworms spend all their lives in tissues and therefore cause persistent eosinophilia. *Wuchereria bancrofti*, *Brugia malayi*, *Loa loa* and *Onchocera volvulus* are the most frequently encountered tissue nematodes in immigrants and travelers. These filarial nematodes complete part of their life cycle in the human host following larval transmission by biting arthropods. After inoculation, the adult offspring called microfilariae mature over three to four months into adult worms and reside in lymphatics and lymph nodes (*Wuchereria bancrofti*, *Brugia malayi*, *Loa loa*) or subcutaneous nodules (*Onchocerca volvulus*). Adult worms produce microfilariae which circulate in the blood (*Wuchereria bancrofti*, *Brugia malayi* and *Loa loa*) or migrate through skin (*Onchocerca volvulus*) where they are ingested by biting insects to complete the cycle. Filariasis usually requires prolonged or intense exposure to the transmitting arthropod. All filarial antigens cross-react with dog heartworm and thus serology for *D. immitis* often suggests the diagnosis. Specific identification depends on demonstrating the microfilariae in skin or blood. Using these diagnostic methods, 40 percent of patients still elude diagnosis and treatment must be empiric. Therapy is based on the geographic location of the immigrant or traveler. The tissue nematodes most commonly associated with eosinophilia in Rhode Island are listed in Table 2.

W. bancrofti and *B. malayi* are small threadlike nematodes found in the lymph nodes and lymphatics of human adults. Mature larvae enter the human host through the mouth-parts of mosquitoes. Following a maturation period of approximately one year the mi-

TABLE 2. Tissue Nematodes

<i>Wuchereria bancrofti</i>
<i>Brugia malayi</i>
<i>Loa loa</i>
<i>Onchocera volvulus</i>
<i>Trichinella spiralis</i>

crofilariae of most species are released nocturnally into the blood where they reach maximal circulatory levels between 12 and 4 AM. Damage to lymphatics caused by adult worms, and the immune response their presence elicits within the host, cause lymphangitis, chronic lymphedema, hydrocele and elephantiasis. Travelers most commonly present with transient recurrent lymphangitis with marked (>1,000) eos/mm² eosinophilia. Occasionally these nematodes cause the tropical pulmonary eosinophilia syndrome. In this syndrome generalized adenopathy is associated with cough, and asthma, and abnormal chest x-ray findings probably secondary to the host's overexuberant immune response to microfilariae. Marked, persistent eosinophilia and elevated IgE usually occur. In the absence of the tropical pulmonary eosinophilia syndrome, the diagnosis of filariasis is made by obtaining day and night bloods for microfilariae. Ivermectin kills microfilariae but does not result in eradication of adult worms. Recurrent therapy is often indicated. The older agent diethylcarbamizine (DEC) may be used but can evoke violent reactions. This adverse reaction to DEC in infected individuals can occasionally be diagnostic.

Loa loa are semi-transparent threadlike nematodes, measuring about 50 mm, transmitted by the horse or deer fly, and endemic in western and central Africa and equatorial Sudan. Although tabanid flies native to the United States are capable of transmitting

loiasis, the disease has never been established here. Loiasis is contracted after larvae penetrate human skin and migrate to connective tissue where they mature over 4-6 months. Adult worms disperse microfilariae into human blood with a peak diurnal periodicity at noon. Symptoms occur as the helminth migrates through the conjunctiva where it can produce acute conjunctivitis or, most commonly, through skin causing transient 5-10 cm localized areas of cutaneous angioedema (calabar swellings) pathognomonic for loiasis. Pronounced eosinophilia is common early in the disease and may reach 30-60 percent of the total peripheral white blood count. Since microfilariae may be difficult to demonstrate in blood, especially in early infection, a marked eosinophilia with a history of calabar swellings may make the diagnosis (as in our case). *D. immitis* titers are usually elevated. Treatment with DEC is usually curative but may need to be repeated. A massive reaction, or calabar swelling occurs characteristically around the site of a dying worm in response to therapy and confirms the diagnosis. Ivermectin has not been shown to be effective.

Onchocerca volvulus causes river blindness, one of the leading causes of blindness worldwide. These filarial helminths reside in skin and are transmitted by the biting female black flies. Following inoculation, infective larvae mature in the skin over approximately three months and produce microfilaria that migrate primarily in the dermis. Onchocercomata, characteristic firm nontender subcutaneous nodules, are formed over months to years by a granulomatous inflammatory reaction evoked by adult worms. The anatomical location of these nodules is frequently determined by the species of fly and

the geographic region in which it is endemic (near head and neck in the Americas or near the hips and legs in Africa). Dermatitis with severe pruritis accompanies microfilarial migration. Lymphadenitis can lead to lymphatic obstruction. Visual impairment is frequent but usually occurs late in the disease. Travelers and immigrants normally present with dermatitis first but if left untreated, acute conjunctivitis, sclerosing keratitis, anterior uveitis or choroiditis will occur. Frank optic nerve atrophy has been described. Slit lamp examination often demonstrates the microfilariae in the cornea and anterior chamber. Diagnosis is based on identification of microfilariae on skin snips or adult worms on excision of onchocercomata. Recently the CDC has developed a specific serologic test for onchocerciasis. Treatment with ivermectin is directed at eradicating microfilariae and must be used yearly. Eradication of adult worms generally requires the use of quite toxic drugs and therefore is often not attempted.

The tissue nematode *Trichinella*, which resides in muscle and classically causes periorbital edema and eosinophilia, is rarely a cause of eosinophilia in returning travelers.

Trematodes

Schistosomiasis caused by *S. mansoni*, *S. japonicum*, *S. haematobium* or *S. mekongi* as well as clonorchiasis and paragonimiasis are the most common trematode etiology of an elevated eosinophil count (Table 3).

People contract schistosomiasis by swimming in fresh water. Fresh water free-swimming cercariae are released in large numbers by the snail intermediate host and penetrate human skin. Acute symptoms called "swimmer's itch" occur with skin penetration.

TABLE 3. Trematodes

<i>Schistosoma mansoni</i>
<i>Schistosoma japonicum</i>
<i>Schistosoma haematobium</i>
<i>Schistosoma mekongi</i>
<i>Clonorchis sinensis</i>
<i>Paragonimus westermani</i>

Following maturation schistosomes reside in vesical and portal venules of the human host. Katayama fever consisting of fever, hepatosplenomegaly and lymphadenopathy may occasionally occur several weeks following massive primary infection and probably represents a generalized hypersensitivity reaction to massive infection. Most people with schistosomiasis have chronic disease. Greater than half of the eggs laid by adult schistosomes remain within the host and chronic disease results from the granulomatous inflammatory response to these trapped eggs in liver, lung and ureters. *Schistosoma mekongi* is the most frequent schistosome species encountered in Rhode Island because of our large Cambodian population. The diagnosis of schistosomiasis is made by examining the stool or urine for ova. Rectal biopsy is occasionally required to diagnose very light infections. A specific serologic test is available from the CDC but is difficult to interpret in immigrant populations.

Clonorchis sinensis, also known as the Chinese or Oriental liver fluke occurs in fish-eating mammals. This helminth requires two intermediate hosts for maturation. Infected snails give off free-swimming cercariae which encyst under scales of fresh-water fish. The human host is infected through ingestion of inadequately cooked or raw fish. Long term infection may result in relapsing cholangitis, pancreatitis and cholangiocarcinoma.

Paragonimiasis is caused by the lung fluke *Paragonimus westermani*. Infected fresh water snails shed cercariae which attach to shellfish, particularly crabs, and are ingested by the human host. Migration of larvae may lead to worm development in ectopic sites including brain, liver, and heart. Symptoms include abdominal pain, hemoptysis, and symptoms and signs referable to ectopic disease. Most commonly, adult worms live in the lungs where they encyst. Golden brown

***Schistosoma mekongi* is the most common schistosome species encountered in Rhode Island because of our large Cambodian population.**

ova may be expectorated in sputum or swallowed and passed in feces.

Diagnosis of paragonimiasis and clonorchiasis is made by demonstrating eggs in the stool or sputum. Most trematode infections can be successfully treated with praziquantel. In cases where the etiology of eosinophilia or other suggestive symptoms of helminth infection is unclear, empiric trial with praziquantel may be useful.

Cestodes

Infections with cestodes or tapeworms are common in immigrants but relatively rare in travelers: they are the least likely parasitic cause of eosinophilia in the traveler. Humans are the definitive hosts for *Diphyllobothrium latum*, *Taenia saginata*, *Taenia solium* and *Hymenolepis nana*. The latter two are also able to utilize man as intermediate host for larval development. In *Echinococcus granulosus* humans are solely intermediate hosts and

cannot support complete helminthic development. Signs and symptoms occur as a result of adult worms in the gastrointestinal tract or, as the result of enlarging encysted larvae in mammalian tissue such as brain, lung and liver. Eosinophilia occurs late in the course of disease at the time of larval migration out of the gastrointestinal tract or when cysts rupture. The cestodes that most commonly cause eosinophilia in the Rhode Island population are listed in Table 4.

Intestinal Tapeworms

Taenia saginata and *Taenia solium*, the beef and pork tapeworms respectively, develop into adult worms in the mammalian gastrointestinal tract following ingestion of encysted larva in poorly cooked meat or pork. Immigrants from Ethiopia, Kenya, Yugoslavia and Muslim countries are commonly infected with *Taenia saginata*. *Taenia solium* is more frequently found in immigrants from Eastern Europe, Spain, Portugal, Central and South America, other African countries, China and India. Both of these helminths are large and may attain lengths of twenty to thirty feet. *Diphyllobothrium latum*, the fish tapeworm, occurs in regions where raw fish is frequently ingested such as Japan, China, Southeast Asia, Baltic countries, Canada and Alaska. These three tapeworms are readily diagnosed by finding characteristic eggs and proglottids in stool. Treatment is accomplished with a single dose of niclosamide following a light meal. Praziquantel is also effective. *Hymenolepis nana*, the dwarf tapeworm, can maintain its life cycle with man acting as the only host. It is therefore occasionally seen in institutionalized patients as well as in people living in unsanitary crowded conditions. Niclosamide is used to

TABLE 4. Cestodes

<i>Taenia saginata</i>
<i>Taenia solium</i> (cysticercosis)
<i>Diphyllobothrium latum</i>
<i>Hymenolepis nana</i>
<i>Echinococcus granulosus</i> (hydatid disease)

cure *H. nana* infection with a long course of 4-5 days required to eradicate all encysted larva. Among the intestinal cestodes, eosinophilia is most common with *H. nana*.

Taenia solium causes the disease cysticercosis when humans serve as the intermediate, rather than the definitive, host. People are most frequently infected following ingestion of eggs from food or water contaminated by human feces. Autoinfection in a person infected with the adult tapeworm also occurs. Following ingestion of eggs, developing larvae penetrate intestinal mucosa and migrate to almost any body tissue, most importantly the central nervous system, where they encyst and become fully infective larvae. In Mexico and parts of South America and Africa cerebral cysts of 2-5 cm are common and can simulate tumor or other neurologic diseases. Patients frequently present with seizures. Three to five years after infection viable cysts degenerate and evoke an inflammatory reaction associated with eosinophilia. Diagnosis is made serologically or by X-rays, especially computerized tomography of the head. Praziquantel effectively kills *T. solium* larva but can cause acute inflammation associated with degeneration of the organism.

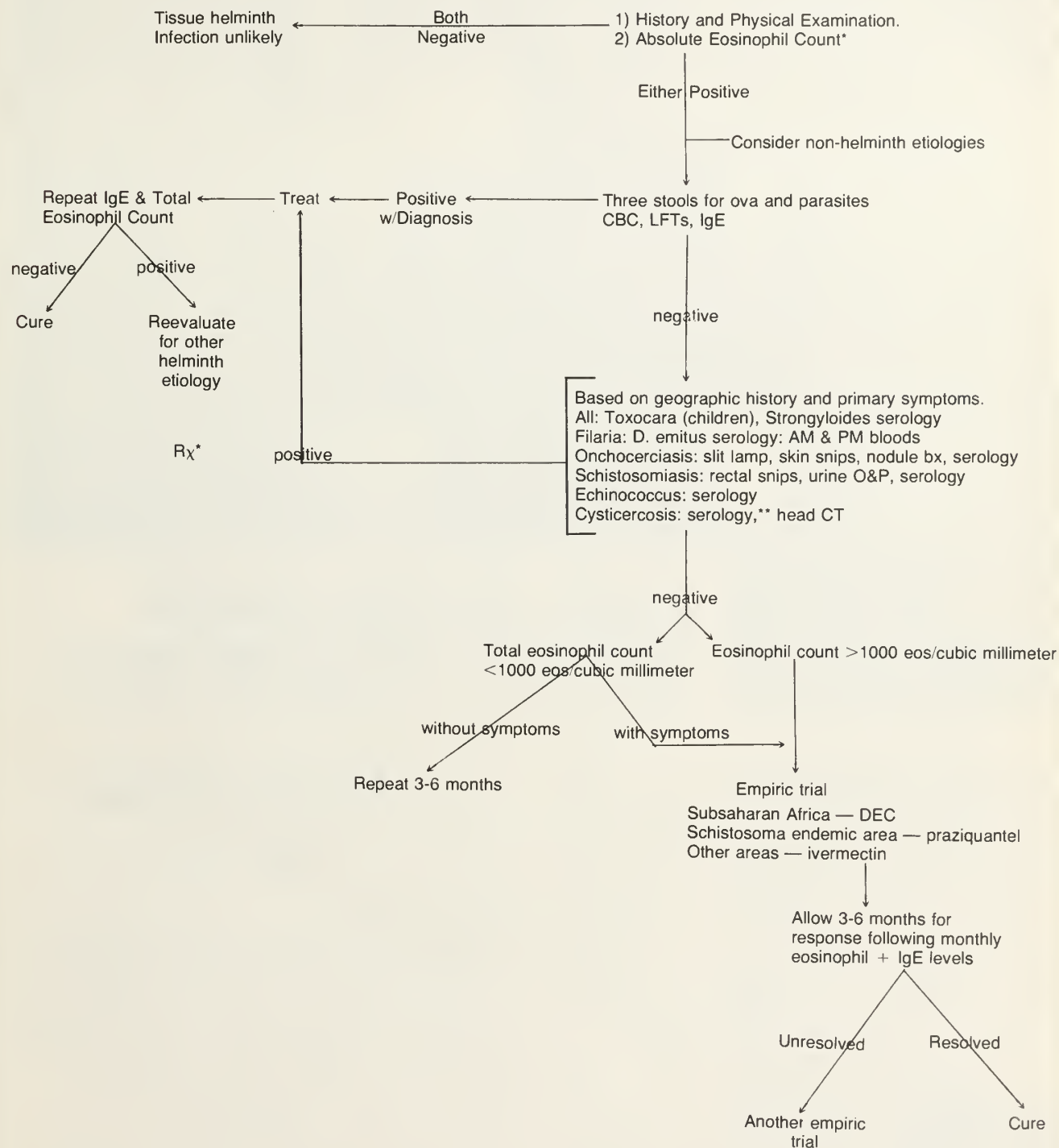
The tapeworm *Echinococcus granulosus* causes echinococcosis or hydatid disease in sheep or cattle farming regions of the world such as Southern Italy, Australia, New Zealand, Argentina, Chile, Uruguay and the Middle East.

Echinococcus granulosus are small helminths whose definitive hosts are dogs. People accidentally become infected following ingestion of contaminated canine feces. The larvae, called oncospheres, then penetrate human mesenteric vessels and develop into hydatid cysts most commonly in liver and lung. These cysts grow slowly at approximately one centimeter per year first causing symptoms by compressing host tissue and eventually causing symptoms associated with rupture. Eosinophilia does not occur except in association with the host's hypersensitivity response to a leaking or ruptured cyst at which time an elevated IgE is also commonly found. Hydatid disease is most frequently diagnosed on radiologic exam of the abdomen or chest. Definitive diagnosis is made through serology. Surgical removal of the intact cysts is the treatment of choice. Recently, praziquantel in combination with albendazole has been used to treat inoperable cases.

Diagnostic Evaluation

The medical evaluation of a traveller or recent immigrant should include an absolute eosinophil count, since using the total white count and the percentage eosinophils to calculate eosinophilia is often very inaccurate (Fig 1 outlines an approach to the evaluation). If the eosinophil count exceeds five hundred, or findings on history or physical exam suggest helminth infection, stool for ova and parasites as well as liver function studies and serum IgE should be obtained. When stool studies are diagnostic (ie, a helminth ova or larvae is found), specific therapy is undertaken followed by a repeat total eosinophil count and IgE to determine cure two to three months later. In a patient whose counts remain el-

TRAVELER OR RECENT IMMIGRANT



* Eosinophil count >1000 requires aggressive workup and definitive treatment

** Immunoblot at CDC

Figure 1

evated further evaluation is required since infection with multiple helminths or other causes of eosinophilia may coexist.

Frequently, even three stools for ova and parasites may be negative or nondiagnostic. Work-up is then based on specific geographic history and presenting symptoms. All patients require serologic screening for toxocara (children) and strongyloides since they are common causes of eosinophilia and stool exams are frequently negative. In patients from filaria endemic regions, *D. immitis* serology may be suggestive and day and night bloods for filariasis diagnostic. Onchocerciasis, echinococcus and cysticercosis can be diagnosed by specific serologies. The diagnosis of schistosomiasis may require urine for ova and parasites (for *S. hematobium*) or rectal snip.

Although tabanid flies native to the United States are capable of transmitting loiasis, the disease has never been established here.

As many as 40-60 percent of patients will elude diagnosis following the preceding workup.¹⁵ At this point empiric treatment based on geographic history is undertaken in patients who are symptomatic or whose absolute eosinophil count exceeds 1000 eos/mm³. To determine cure following empiric therapy, the eosinophil count and IgE levels should be reevaluated three and six months after treatment. A second or third empiric trial with a new drug is occasionally required. Patients who elude diagnosis but are asymptomatic and have mild eosinophilia (<1000 eos/mm³) should be reevaluated in three to six months as outlined above.

The work-up for eosinophilia is

somewhat more complicated than most other medical conditions since it requires some familiarity with clinical tropical medicine. For help or assistance please call the Traveler's Clinic at The Miriam Hospital (401) 274-3700 Ext. 4075 or Memorial Hospital of Rhode Island (401) 722-6000 Ext. 2545.

References

- 1 Mahmoud AAF. In: Eosinophilia in Tropical and Geographic Medicine. Warren KS and Mahmoud AAF, eds. McGraw Hill, NY, NY. 1984.
- 2 Nutman TB, Ossesen EA, Ienq S, Samuels J, Kimball E, Lutkoski M, Zierdt W, Gam A, Neva F. Eosinophilia in southeast Asian refugees: Evaluation at a referral center. J. Infect. Dis. Vol. 155, No. 2 1987:309-313.
- 3 Butterworth AE, David J. Eosinophil function. NEJM 1981;304:154-156.
- 4 Weller PF, Geotzl EJ. The human eosinophil. A.J. Pathol. 1980; Vol. 100, No. 3:793-819.
- 5 Mahmoud AAF and Avsten KF. The eosinophil in health and disease. Grave and Stratton; New York, 1979.
- 6 Gleich GJ. The eosinophil: New aspects of structure and function. J Allergy Clin Immunol. 60(1):73-82, 1977.
- 7 Horii Y, Ishii A, Owhashi M. In vitro and in vivo induction of neutrophil and eosinophil chemotactic responses by *Schistosoma japonicum cercariae*. Am J Trop Med Hyg, 513-518, 1985.
- 8 Mahmoud AAF. In: Geographic Medicine for the Practitioner. Warren KS and Mahmoud AAF, Eds. The University of Chicago Press, Chicago, IL, 1978.
- 9 Olds GR. Eosinophilia in returning travelers. (Unpublished data).
- 10 Pelletier LL, Baker CB, Gam AA, Nutman TB, Neva FA. Diagnosis and evaluation of treatment of chronic strongyloides in the prisoners of war. J. Infect. Dis. 1988; Vol. 157, No. 3:573-576.
- 11 Genta RM, et al. Strongyloides in Veterans of Vietnam and other wars. JAMA 1987; Vol. 258, No. 1:49-52.
- 12 Gann AA, Neva FA, Krotoski WA. Comparative specificity of ELISA and IHA for serodiagnosis of strongyloidiasis with larval antigens. Am J Trop Med Hyg, (37)1988:157-161.
- 13 VanDellen RG, Ottensen EA, Gocke G, Neafie R. Loa Loa. JAMA, 1985; 253:1924-1925.
- 14 Harries AD, et al. Eosinophilia in caucasians returning from the tropics. Trans. of Roy. Soc. Trop. Med. Hyg. 1986;80:327-328.

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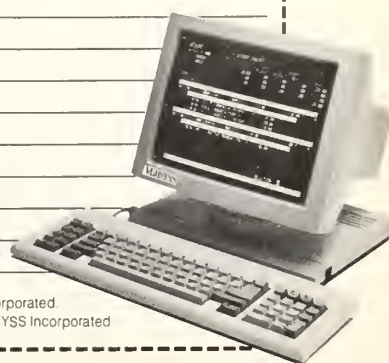
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Traveler's Diarrhea: Methods of Prevention and Treatment

Steven M. Opal, MD
Peter M. Wiest, MD
G. Richard Olds, MD

Traveler's diarrhea can often be avoided by following safe food and water practices while traveling in developing countries. The water supply available to the traveler is the single greatest hazard.

Traveler's diarrhea is the most common medical complication of international travel. This illness is well-known to travelers and is referred to by a variety of colorful names including "Tourista," "Montezuma's Revenge," "Aztec Two-Step," "Rome Runs,"

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"Turkey Trots," etc. While diarrhea represents little more than a nuisance to most travelers, up to 40 percent of travelers will need to change their itinerary or cancel the remainder of their trip as a direct result of acquiring diarrhea during travel. Traveler's diarrhea remains a major concern of international travelers and has stimulated a variety of efforts to prevent this troublesome illness.^{1,2}

Traveler's diarrhea is primarily seen in individuals from developed countries, such as the United States and Europe, who travel to developing countries where food and water sanitation are poor. Travelers from developed countries have little or no intestinal immunity to a variety of common enteropathogens which are prevalent in developing countries. Traveler's diarrhea is rarely a problem for inhabitants of developing countries when traveling to other developing nations or to the United States or Europe. The risk of acquiring traveler's diarrhea varies widely depending

upon the travel itinerary, dietary habits, and duration of travel. Travelers who eat exclusively in private homes while traveling have a low risk; travelers who eat at major hotel chain restaurants have an intermediate risk; and travelers who eat at small restaurants, cafeterias, and street vendors have a great risk of acquiring diarrhea.³

Studies done on Peace Corps workers in Latin America or Africa have demonstrated that the risk of traveler's diarrhea is approximately 20 percent per week for the first five weeks of travel if no preventive measures are taken.⁴ The risk of acquiring diarrhea can be substantially diminished by a variety of dietary precautions and by the judicious use of pharmacologic agents in the

ABBREVIATIONS USED:

ETEC: Enterotoxin-producing *E. coli*

ORS: Oral rehydration solution

SMX-TMP: Trimethoprim-sulfamethoxazole

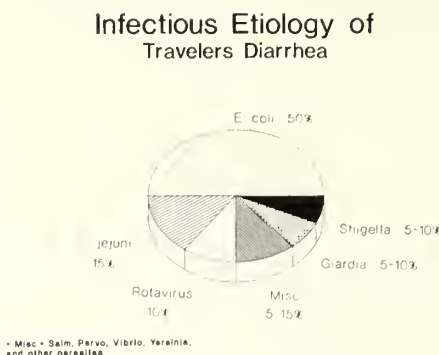
prevention and early treatment of traveler's diarrhea.

The Causes of Traveler's Diarrhea

Numerous studies over the past twenty years have attempted to analyze the microbiology of traveler's diarrhea.^{2, 3, 5, 6} Despite regional variations in prevalence of specific pathogens, the overall pattern of etiologic agents causing traveler's diarrhea in the Far East, Africa, and South America remains similar. The most common organisms implicated in traveler's diarrhea are depicted in Figure 1. At least 50 percent of all cases of traveler's diarrhea are due to *Escherichia coli*.^{3, 5} While *Escherichia coli* may produce diarrhea by a variety of mechanisms, enterotoxin producing *E. coli* (ETEC) is by far the most common cause of traveler's diarrhea. A heat-labile enterotoxin (LT toxin) or a heat-stable toxin (ST toxin) is produced by enterotoxigenic *E. coli*. Up to a third of isolates will express both toxins simultaneously.³ While each toxin has a different molecular mechanism of action, both toxins inhibit the absorption of water and solutes as well as cause secretion of fluid into the intestinal lumen resulting in watery diarrhea. After an incubation period of 24-48 hours, enterotoxigenic *E. coli* will produce diarrhea associated with cramping and low-grade fever which will persist for 4-7 days. The diarrhea may be severe resulting in up to 10-12 unformed stools per day. This form of diarrhea is noninflammatory and is not associated with white blood cells or blood in the stool.

Other common causes of traveler's diarrhea include *Campylobacter jejuni* and *Shigella spp.* *Campylobacter jejuni* is a common organism found in multiple animal sources and is a potential risk to travelers who eat inade-

Figure 1.



quately prepared food. Additionally, this organism is frequently found in surface waters and may cause waterborne outbreaks from inadequately purified water. *Campylobacter enteritis* may present as either a secretory, non-inflammatory diarrhea or as an invasive diarrhea associated with fever, severe cramps and white blood cells and blood in the stool (dysentery). Shigellosis, on the other hand, is almost always associated with an inflammatory diarrhea and is the major cause of bacillary dysentery. Shigellosis is often severe and may be an incapacitating illness frequently necessitating hospitalization. *Shigella spp.* invade and destroy the colonic epithelial cells leading to severe cramping, high fever, tenesmus, and bloody diarrhea. Shigellosis is highly transmissible and person to person transmission is common. Transmission of Shigellosis by arthropod contamination of foods (flies and cockroaches) also occurs in endemic areas with poor sanitation.^{3, 5, 6}

Two other common causes of traveler's diarrhea include rotavirus enteritis as well as *Giardia lamblia* infection. Rotavirus is the most common cause of infantile diarrhea throughout the world. Recently, it has been recognized that rotavirus is a common cause of traveler's diarrhea in adults.³ Rotavirus is generally acquired through contaminated food or

water supplies and results in a noninflammatory, watery diarrhea. The organism invades the small intestinal villi resulting in loss of villus tips and blunting of the villi throughout the small intestine. This disrupts the primary absorptive surface of the small intestine resulting in a watery diarrhea.

Giardia lamblia is a ubiquitous protozoan parasite which frequently contaminates water supplies in developing nations. The organism produces a cyst which is relatively resistant to chlorination and may contaminate municipal water supplies despite chlorination procedures. *Giardia lamblia* causes a secretory diarrhea associated with abdominal bloating and belching and flatulence which may persist for several weeks. The infection is often complicated by acquired lactase deficiency which may prolong the symptomatic period of diarrhea. Giardiasis may be severe resulting in weight loss and malabsorption in immunocompromised patients and achlorhydric patients.

Other causes of traveler's diarrhea are indicated in Figure 1.

The Prevention of Traveler's Diarrhea

The prudent traveler may greatly diminish the risk of acquiring traveler's diarrhea by strictly adhering to guidelines for safe food and water ingestion during international travel. The water supply available to the traveler is the single greatest hazard to acquiring diarrhea. Tap water and other municipal water supplies are often unsafe for consumption in many developing countries. The only absolutely safe drinking water for the traveler is water that has been boiled for five minutes or greater prior to serving. Hot beverages such as coffee and tea served piping hot is considered

safe. Boiling water for personal use is rather cumbersome and may be difficult for adventurous travelers who frequent non-urban areas in developing countries. Other sources of water which are considered safe include carbonated beverages (soda pop), bottled and commercially prepared and labelled sparkling waters and alcoholic beverages. Carbonated drinks are usually safe owing to the low acidity associated with carbonation which inhibits the growth of enteric pathogens. Carbonated beverages are best served at room temperature in their original containers and without ice added. Alcoholic beverages including beer and wine as well as liquor are considered safe for consumption as well.⁷

Two additional methods of water purification during travel include water filtration or halogenation. A number of commercially available water filters are sold in developing countries. These filters have not been rigorously tested in controlled trials to determine their efficacy. Additionally, the filters are of variable quality depending on the manufacturer and the specific

system. Water purity cannot be guaranteed using water filters and should be considered a less desirable alternative for potable water when safer water supplies are unavailable.

Halogenation of water prior to consumption is a time-honored and effective means of producing a safe water supply if proper halogenation technique is followed assiduously. In practice, few travelers adhere to the stringent requirements for water preparation by halogenation and this often leads to the ingestion of potential enteropathogens. Details of various methods of halogenation are given in Table 1. The efficacy of halogenation depends upon numerous factors including water turbidity, pH, salinity, and temperature. Halogenation is less efficient in very cold water and requires greater contact time in order to be effective. This is particularly problematic in eradicating *Giardia lamblia* cysts. These cysts are relatively resistant to halogenation in cold water which is, therefore, a major limitation to this method of water purification. Grossly turbid water should be strained through a clean cloth

prior to halogenation to remove particulate matter which interferes with halogenation. Halogenated water supplies are most effective if conducted on a large scale with a prolonged contact time prior to water ingestion. This may be appropriate for trading posts, travel stations, and permanent camps in rural areas in developing countries.

Common errors made by travelers which result in the acquisition of water-borne enteric pathogens include: (1) adding ice chips to otherwise safe water (freezing preserves but does not kill enteric pathogens and ice is no safer than the tap water); (2) adding alcohol to water in an attempt to "sterilize" water (alcohol will inhibit but not kill a variety of enteric organisms); and (3) using tap water for tooth brushing or for washing (a small supply of bottled water should be used for tooth brushing). A safe water supply is taken for granted in the United States (except in Bristol County, Rhode Island) but is frequently unavailable in developing countries. International travelers should be advised to follow appropriate precautions to

Table 1. Halogenation of Water Supplies.

Halogen	Methods	Comments
Tetraglycine Hydroperiodide (Potable Aqua®)	Add 2 tablets to 1 qt of water for 30 min at 20°C (room temp) mix every 5 min.	Probably the best method, not as effective for very cold water.
Iodine (Globaline®)	Add 2 tablets to 1 qt of water for 30 min at 20°C, mix every 5 min.	Widely used, very effective.
Chlorine (Halazone®)	Add 5 tablets to 1 qt of water for 30 min at 20°C, mix every 5 min.	Outdated halazone is less effective.
Chlorine bleach (Clorox®)	Add 2 drops (0.1 ml) of 5% chlorine bleach to 1 qt. of clear water and allow to stand for 30 min. Double the dose for turbid water.	Less effective for very cold water.

assure a safe water supply.

Most travelers are cognizant of the risks of an unsafe water supply yet expose themselves to great risk through the ingestion of inadequately prepared foods. Uncooked foods, such as fresh fruits and salads, are often contaminated with potentially pathogenic microorganisms and pose a significant risk for traveler's diarrhea. These foods are best avoided entirely while traveling in developing countries. Fruits and vegetables that are purchased fresh and then peeled by the traveler prior to consumption are generally safe. Food is considered safe for consumption if cooked and then served hot. The often stated adage, "If you can't peel it, boil it, or cook it, forget it!" remains cogent advice for the international traveler. Breads are generally safe for consumption but pastries with icing may not be and should be avoided. Fresh water fish and seafood dishes should only be ingested if well-cooked. Dairy products may not be adequately pasteurized and should be avoided.⁷

Travelers who eat exclusively in private homes while traveling have a low risk; travelers who eat at major hotel chain restaurants have an intermediate risk; and travelers who eat at small restaurants, cafeterias, and street vendors have a great risk of acquiring diarrhea.

The potential value of strict adherence to safe food and water practices while traveling in developing countries has recently been demonstrated in a study of Swiss travelers to the tropics.⁸ The incidence of traveler's diarrhea varied from 6.1 percent up to 28.6 percent and was directly propor-

tional to the number of dietary indiscretions during the first three days of travel. These data demonstrate that careful dietary controls will significantly diminish but not entirely eliminate traveler's diarrhea in susceptible populations.^{7, 8}

The Prevention of Traveler's Diarrhea by Pharmacologic Methods

Travelers have often resorted to a variety of prescription and non-prescription drugs to prevent traveler's diarrhea. In controlled trials no beneficial prophylactic effect has been demonstrated with entero-vioform, lactobacilli, antimotility drugs, or ethacridine. Drugs such as entero-vioform were widely used in the past because of the widespread belief that these drugs prevented traveler's diarrhea. This drug has also been associated with irreversible eye injury when taken for prolonged periods and is now contraindicated in the prevention of traveler's diarrhea.^{3, 9}

A widely available, non-prescription agent that is of some benefit in preventing traveler's diarrhea is bismuth subsalicylate (Pepto-Bismol®). In placebo controlled trials, bismuth subsalicylate had a protective efficacy of approximately 60 percent in preventing traveler's diarrhea in short-term travelers to Mexico.¹⁰ Bismuth subsalicylate was well-tolerated but required exceedingly large doses (60 ml p.o. Q.I.D. in order to provide protection). This volume of bismuth subsalicylate liquid is quite inconvenient and not suitable for prolonged periods. Bismuth subsalicylate tablets (300 mg/tablet) at a dose of two tablets four times a day has also been shown to be of benefit in preventing traveler's diarrhea.^{4, 11} This formulation is convenient in that the tablets are chewable and do not require refrigeration. The mechanism by

which bismuth subsalicylate provides protection against traveler's diarrhea is complex. Bismuth itself has some anti-bacterial activity. The salicylate component provides some protection against the secretory mechanism of enterotoxin induced diarrhea. Bismuth subsalicylate has also been shown to interfere with the binding of enterotoxigenic *E. coli* to intestinal epithelium thereby preventing colonization and infection. The side effects of bismuth subsalicylate are generally mild including discoloration of stool, occasional constipation, and elevation of the blood salicylate level. This may complicate the management of patients receiving high dose salicylates, oral anticoagulants or uricosurics. Bismuth subsalicylate is also useful in the treatment of traveler's diarrhea.¹¹

Antimicrobial prophylaxis against traveler's diarrhea has been successfully developed with a number of antimicrobial agents.^{9, 12, 13} Antimicrobial agents known to be effective in preventing traveler's diarrhea on the basis of placebo controlled trials are listed in Table 2.

Antimicrobial chemoprophylaxis should only be given for short-term travelers.

There are numerous potential problems associated with antimicrobial chemoprophylaxis against traveler's diarrhea including side effects of the medication, promotion of antimicrobial resistance,¹⁴ expense and inconvenience, drug interactions, and candidal vaginitis in women. A national consensus conference held recently on traveler's diarrhea recommended that antimicrobial prophylaxis not be given for international travelers with the exception of a few special situa-

Table 2. Effective Antimicrobial Agents in the Prevention of Traveler's Diarrhea

Antimicrobial Agent	Dose	Comments
Doxycycline	100 mg daily	Effective even against tetracycline-resistant organisms, multiple potential side effects.
Trimethoprim-Sulfamethoxazole (SMX-TMP)	160 mg/800 mg daily	Highly effective, hypersensitivity reactions may occur, antibiotic resistance is increasing.
Trimethoprim	200 mg daily	Effective but less so than SMX-TMP.
Norfloxacin	400 mg daily	Well-tolerated, highly effective.

tions.⁶ Potential indications for antimicrobial prophylaxis against traveler's diarrhea were considered for travelers on essential missions (State Department visits), international travel in severely immunocompromised hosts, and patients in whom diarrhea poses a great risk (elderly, patients with cardiovascular disease, and patients with renal dysfunction). Antimicrobial chemoprophylaxis should only be given for short-term travelers and it would not be appropriate for travelers who plan to spend greater than two weeks in developing countries.^{4, 6}

The Treatment of Traveler's Diarrhea

The only required treatment for all forms of diarrhea, regardless of its cause, is fluid therapy to replenish the extracellular volume. Patients are capable of absorbing fluid and electrolytes even in the midst of severe secretory diarrhea. A glucose and electrolyte solution is widely available throughout the developing world in the form of oral rehydration solution (ORS) developed by the World Health Organization. This oral rehydration regimen includes 5 grams of sodium chloride, 2.5 grams of NaHCO₃, 1.5 grams of KCL and 20 grams of glucose. This oral rehydration solution is provided in prepackaged form which is mixed with one li-

ter of safe water. A satisfactory solution may be prepared by adding 4 level tablespoons of table sugar with 1/2 teaspoon of table salt and 1 teaspoon of sodium bicarbonate (baking soda) in 1 liter of boiled water. This solution should be taken in addition to a citrus fruit or banana to provide a potassium source. Numerous commercially available electrolyte solutions (Gatorade, Pedialyte, or Stop-Trot) are also effective oral rehydration solutions. These solutions should be taken as frequent small servings in addition to a safe water supply as long as the patient remains thirsty. The oral rehydration solution is safe and effective in infants and small children as well as adults.¹⁵

Other effective methods of treating traveler's diarrhea include bismuth subsalicylate as well as anti-motility agents. Bismuth subsalicylate is effective as both a preventive measure and a treatment method.^{9, 10} Anti-motility agents which inhibit gastrointestinal peristalsis such as diphenoxylate (Lomotil®) and loperamide (Imodium®) have both been shown to be effective and safe in the treatment of uncomplicated traveler's diarrhea. Anti-motility agents have a rapid onset of action and are more effective than bismuth subsalicylate in the first 48 hours of diarrhea.¹¹ Anti-motility agents are

widely used for symptomatic relief of watery diarrhea in travelers as a means of rapidly controlling symptoms of most forms of traveler's diarrhea. Anti-motility agents are unsafe in infants and small children and should not be given to travelers who experience high fever or dysentery owing to the potential risk of exacerbating shigellosis and other forms of invasive diarrhea.^{4, 11} The traveler's clinics at the Miriam and Memorial Hospitals generally recommend that prescription anti-motility agents be given only to adults with mild diarrhea. These drugs should be given concomitantly with empiric antimicrobial agents which specifically treat enteric organisms.

Should traveler's diarrhea develop, fluid replacement is the principal therapeutic modality.

Empiric use of antimicrobial agents during the early phases of traveler's diarrhea has been shown to be highly effective in shortening the duration of traveler's diarrhea.^{16, 17} Numerous antimicrobial agents have been shown to be of potential utility in this setting. The most widely used agents include trimethoprim-sulfamethoxazole, 160mg/800mg, (1 double strength tablet) every 12 hours for 5 days; doxycycline, 100

mg twice daily for 5 days; norfloxacin, 400 mg, twice daily; ciprofloxacin, 500 mg, twice daily for 5 days; or furazolidone, 100 mg, 4 times a day for 5 days. All these antimicrobial agents have been shown to be of value in placebo-controlled trials of early empiric therapy in the treatment of traveler's diarrhea.^{9, 13, 16, 17} Trimethoprim-sulfamethoxazole is currently the most widely used antibiotic for this indication. However, the increasing prevalence of sulfa and trimethoprim resistant organisms in Brazil, Argentina, the Middle East and some areas in Indochina may limit the utility of this agent in the near future. Similarly, widespread tetracycline resistance may limit the value of doxycycline in traveler's diarrhea.¹⁴ The newer quinolone agents, norfloxacin or ciprofloxacin, provide several potential advantages in the treatment of traveler's diarrhea. These agents are highly effective against a wide variety of enteric pathogens including campylobacter and yersinia infections. Resistance to the quinolones infrequently develops during therapy and no plasmid-mediated resistance to the quinolone agents has yet been discovered. This will limit the rapidity with which quinolone resistance develops among enteric pathogens.^{13, 16} Another factor to consider when prescribing antibiotics is their relative cost. The current cost of a five day course of a quinolone antibiotic is \$20-30 dollars. A comparable course of trimethoprim-sulfamethoxazole costs \$3-6. Furazolidone has the potential advantage of treating giardiasis in addition to a variety of bacterial enteropathogens. Gastrointestinal side effects in addition to an antabuse effect limits the acceptability of this agent as standard treatment for traveler's diarrhea.⁶

Summary

Traveler's diarrhea can often be avoided by following safe food and water practices while traveling in developing countries. Prophylactic agents are generally not indicated in the prevention of traveler's diarrhea. Should traveler's diarrhea develop, fluid replacement is the principal therapeutic modality. Other useful treatments include bismuth subsalicylate or anti-motility agents such as loperamide or diphenoxylate. Early empiric use of antimicrobial agents including trimethoprim-sulfamethoxazole or quinolone agents offers an excellent means of treating traveler's diarrhea and preventing its potential complications. Travelers who develop dysentery, high fever, or prolonged diarrhea lasting more than 10-14 days should seek medical attention for specific diagnosis and appropriate antimicrobial therapy.

References

- Hilton E, Edwards B, Singer C. Reported illness and compliance in U.S. travelers attending an immunization facility. *Archives of Internal Medicine* 1989;149:178-179.
- Steffen R, Rickenback M, Wilhelm U, Helminger A and Schar M. Health problems after travel to developing countries. *Journal of Infectious Diseases* 1987;156:84-90.
- MacDonald KL and Cohen ML. Epidemiology of traveler's diarrhea: current perspectives. *Reviews of Infectious Diseases* 1986;8 (Supplement 2):S117-S121.
- Reves RR, Johnson PC, Ericsson CD and DuPont HL. A cost effectiveness comparison of the use of antimicrobial agents for treatment or prophylaxis of travelers' diarrhea. *Archives of Internal Medicine* 1988;148:2421-2427.
- Black RE. Pathogens that cause traveler's diarrhea in Latin America and Africa. *Reviews of Infectious Diseases* 1986;8 (Supplement 2):S131-S135.
- National Institutes of Health Consensus Conference. Consensus development conference statement on traveler's diarrhea. *Reviews of Infectious Diseases* 1986;8 (Supplement 2):S227-S233.
- Blaser MJ. Environmental interventions for the prevention of travelers' diarrhea. *Reviews of Infectious Diseases* 8; (Supplement 2):S142-S150.
- Kozicki M, Steffen R, and Schar, M. "Boil it, cook it, peel it, or forget it": Does this prevent travellers' diarrhea? *International Journal of Epidemiology* 1985;14:169-172.
- Steffen R, Heusser R, Tschopp A and DuPont HL. Efficacy and side effects of six agents in the self-treatment of travelers' diarrhea. *Travel Medicine International* 1988;153-158.
- DuPont HL, Sullivan P, Evans DG, Pickering LK, Evans DJ, Vollet JJ, Ericsson CD, Ackerman PB, and Tjoa WS. Prevention of traveler's diarrhea: prophylactic administration of bismuth subsalicylate. *Journal of the American Medical Association* 1980;243:237-241.
- Johnson PC, Ericsson CD, DuPont HL, Morgan DR, Bitsura JAM and Wood LV. Comparison of loperamide with bismuth subsalicylate for the treatment of acute travelers' diarrhea. *Journal of The American Medical Association* 1986;255:757-760.
- Sack DA, Kaminsky DC, Sack RB, Itotia JN, Arthur RR, Kapikian AZ, Orskov F and Orskov I. Prophylactic doxycycline for traveler's diarrhea: results of a prospective double-blind study of Peace Corps volunteers in Kenya. *New England Journal of Medicine* 1978;298:758-763.
- Johnson PC, Ericsson CD, Morgan DR, DuPont HL and Cabada FJ. Lack of emergence of resistant fecal flora during successful prophylaxis of traveler's diarrhea with norfloxacin. *Antimicrobial Agents and Chemotherapy* 1986;30:671-674.
- Murray BE. Resistance of Shigella, Salmonella, and other selected enteric pathogens to antimicrobial agents. *Reviews of Infectious Diseases* 1986;8 (Supplement 2):S172-S181.
- Banwell JG. Treatment of traveler's diarrhea: Fluid and dietary management. *Reviews of Infectious Diseases* 1986;8 (Supplement 2):S182-S187.
- Ericsson CD, Johnson PC, DuPont HL, Morgan DR, Bitsura JAM and De La Cabada, FJ. Ciprofloxacin or trimethoprim-sulfamethoxazole as initial therapy for travelers' diarrhea. *Annals of Internal Medicine* 1987;106:216-222.
- DuPont HL, Reves RR, Galindo E, Sullivan PS, Wood LV and Mediola JG. Treatment of travelers' diarrhea with trimethoprim/sulfamethoxazole and with trimethoprim alone. *New England Journal of Medicine* 1982;307:841-844.

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Malaria: The Deadly Threat From Overseas

Peter M. Wiest, MD
Steven M. Opal, MD
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It is estimated that 8 to 10 million Americans travel each year to malaria-endemic areas. Furthermore, thousands of individuals from such endemic areas migrate to the United States.

The following case occurred in the summer of 1989 in Rhode Island:

A 38-year-old male who had recently traveled to West Africa visited a local emergency room on a Friday evening complaining of fevers and chills. The patient stated that he felt he had malaria since his febrile episode was sim-

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ilar to those that he experienced as a young man while growing up in Africa. Additional symptoms included crampy abdominal pain and loose stools. Physical examination revealed only a low-grade temperature. A complete blood count was reported as normal and a stool sample was sent for culture. He was discharged from the emergency room with the possible diagnosis of salmonellosis.

Over the weekend his relatives and friends did not see him nor could they contact him at his apartment. At the request of the family the manager entered that apartment and found the man dead. Autopsy revealed that the cause of death was cerebral malaria. Review of the peripheral blood smear obtained during the emergency room visit found numerous ring forms in the red blood cells consistent with *Plasmodium falciparum* malaria.

This case illustrates several important points regarding malaria in Rhode Island. First and foremost, cases of malaria may be

seen by Rhode Island physicians. It is estimated that 8 to 10 million Americans travel each year to malaria-endemic areas. Furthermore, thousands of individuals from such endemic areas migrate to the United States. It is therefore likely that a Rhode Island physician will see patients who have recently traveled overseas. In fact, from 1987 to 1989, over 30 cases of malaria have been seen by physicians at the Traveler's Clinics at the Miriam Hospital and the Memorial Hospital. This case also emphasizes that a travel history is essential whenever a patient is being evaluated for a febrile illness. If the patient has traveled to any tropical or subtropical land and has a fever, think malaria!

A second point emphasized by this case is the difficulty of suspecting malaria experienced by physicians who are unfamiliar

ABBREVIATIONS USED:

DEET: *N, N diethylmetatoluamide*

P.: *Plasmodium*

with the disease. This point is described in the article entitled "Malaria — The Mime."¹ As with syphilis and today with the human immunodeficiency virus, the symptoms of malaria can present in many different and subtle ways. High spiking fevers, chills, the "flu," diarrhea, lower abdominal pain, confusion and fatigue allegedly from jet lag are just a few of the clinical presentations of malaria seen by physicians at the Traveler's Clinics. Thus a physician must have a high index of suspicion for malaria whenever a traveler returns from overseas. Moreover, as this case illustrates, abdominal pain and diarrhea may be seen in up to 40 percent of Americans who contract malaria.

Lastly, this case dramatically demonstrates that malaria can kill. It is estimated that 400 million cases of malaria occur worldwide each year. Of these, 2 to 3 million individuals die, with a mortality rate of less than one percent. Unfortunately, in the United States, the mortality rate approaches 10 percent. Thus, despite the technological advances in medicine, a patient is more likely to succumb to malaria in the United States than if the same patient became ill in a grass shack in Africa. Physicians overseas think about malaria and initiate treatment early. In the United States, however, physicians often delay in making the diagnosis of malaria and, therefore, the mortality rate rises.

Epidemiology

Malaria is caused by the protozoan parasite *Plasmodium*. Four species exist in man: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*.^{2,4} Transmission of malaria to humans is achieved by the bite of an infected Anopheles mosquito. Transmission can also occur, though rarely, through blood transfusions, needle-sharing

among intravenous drug users as well as congenital transmission from mother to fetus.

Malaria is found throughout the developing world where Rhode Islanders are increasingly traveling these days for adventure and business. In 1988 alone, over 2,000 Rhode Islanders were seen in the Traveler's Clinics at the Miriam and Memorial Hospitals prior to trips to malaria-endemic areas. These regions include Central and South America, the Caribbean Islands, sub-Saharan Africa, the Middle East, the Indian subcontinent, Southeast Asia and Oceania.

Pathogenesis

Infection is acquired when a female Anopheles mosquito inoculates a human with sporozoites. These organisms rapidly enter hepatic cells, multiply, and rupture into the circulation as merozoites. These parasites then invade erythrocytes and undergo asexual reproduction producing multinucleated schizonts. The erythrocyte ruptures releasing merozoites which again infect other red blood cells. This cycle continually repeats. Some of the parasites, however, mature into male and female gametocytes. Upon ingestion by a female mosquito, gametocytes mate and eventually generate sporozoites which are again infective for humans.

In *P. falciparum* and *P. malariae*, all of the merozoites leave the liver within weeks of the initial infection. For *P. vivax* and *P. ovale*, however, the hepatic forms may remain in the liver for months and even years. At any time thereafter, these organisms can come out of hiding in the liver, infect red blood cells and cause a relapse.

Clinical Presentation

The incubation period from the

introduction of infection to the first symptom ranges from 6 to 30 days depending on the species of malaria. Typically, an infected individual complains initially of flu-like symptoms including headache, fatigue, feverish feeling, chills, malaise, nausea, anorexia and diarrhea. With time the patient develops the classic symptoms of malaria: chills and fever followed by marked diaphoresis. These paroxysms occur every 48 hours for *P. vivax* and *P. ovale*, 72 hours for *P. malariae*, but are usually irregular for *P. falciparum*.

Abnormal laboratory findings may include hemolytic anemia, thrombocytopenia, and elevation of liver function tests.

Periodicity in the fever pattern is the exception rather than the rule. Most travelers present with a variable fever pattern prior to development of periodicity. Therefore, it is essential that a physician consider malaria in the differential for a febrile traveler, even if the classical febrile cycles are not present.

Physical examination may reveal sinus tachycardia, splenomegaly, hepatomegaly, mild jaundice, abdominal tenderness, and scattered rales on auscultation. Abnormal laboratory findings may include hemolytic anemia, thrombocytopenia, and elevation of liver function tests. As the initial case points out, however, malaria can be present without laboratory abnormalities even hours before death.

Complications of malaria are primarily due to infections with *P. falciparum*. This is usually associated with high grade parasitemia, with greater than 5 percent of red blood cells infected with

malaria. The most serious complication is cerebral malaria. Symptoms may include disorientation, psychosis, seizures, stupor, coma and focal abnormalities. Edema is not typically seen, and corticosteroids are not indicated for treatment of cerebral malaria.⁵ Other systemic complications include renal dysfunction, pulmonary edema, and hypoglycemia.

Diagnosis

The only definitive means to diagnose malaria is to demonstrate the parasite in a peripheral blood film. When the diagnosis of malaria is entertained, both a thick and thin blood smear should be obtained. Unfortunately, in the United States, the diagnosis is often made by the medical technologist when a white blood cell differential is being performed for a febrile patient.

The thin blood smear allows identification of the species of *Plasmodium* as well as demonstrates the presence of the parasite in more heavily-infected individuals. In lightly infected people the thick blood smear is a concentration technique allowing one to determine if an individual is infected or not. If the initial smears are negative it is important to repeat blood smears 2-3 times per day for several days since cyclic variation of the parasitemia is seen with all malaria species.

If malaria is identified on a peripheral blood smear, it is necessary for a physician to decide if a patient is infected with *P. falciparum* (the only species that kills), or another species. If the patient is infected with *P. falciparum*, he should be admitted promptly to the hospital and treated since complications can rapidly occur. In contrast, if a non-falciparum species is found, the individual may usually be treated on an outpatient basis. When in doubt, the patient should be hospitalized and treated for presumed falciparum malaria.

Morphological features that allow one to distinguish among the four species of malaria are presented in Table 1 and textbooks.²⁻⁴ Criteria suggestive of *P. falciparum* include a predominance of ring forms (Figure 1), doubly infected red blood cells and banana-shaped gametocytes. The presence of schizonts (multinucleated parasites) in red blood cells is very rarely seen and then only in very high parasitemias. Furthermore, red blood cells are not enlarged and pink stippling of the cytoplasm (Schuffner's dots), which is seen in *P. vivax* and *P. ovale*, does not occur.

Prevention of Malaria

To avoid malaria, travelers should be advised to reduce contact with mosquitoes which bite primarily at night. Such measures include remaining in screened areas, us-

ing mosquito nets, wearing clothes that cover most of the body, and using an insect repellent containing at least 30 percent N, N diethylmetatoluamide (DEET), the active ingredient.

Chemoprophylaxis of malaria in travelers has become complex since development of chloroquine-resistant falciparum malaria. Chloroquine is the most effective agent used to prevent infection with *P. vivax*, *P. ovale*, *P. malariae* and chloroquine-susceptible *P. falciparum* (Table 2).

Figure 1. High-powered view of a thin blood smear with two erythrocytes infected with ring forms of *Plasmodium falciparum*. Note that one of the red blood cells is doubly infected. This is highly suggestive of *P. falciparum*.

Table 1 Diagnostic features of malaria on thin blood smears.

Species	Morphological Characteristics ¹	
	Infected Red Blood Cells	Parasite
<i>P. falciparum</i>	normal-sized RBC, multiply-infected RBC, can achieve high parasitemia	rings predominant, banana-shaped gametocyte (diagnostic)
<i>P. vivax</i>	enlarged RBC, Schurrner's dots	schizont present, ameboid cytoplasm
<i>P. ovale</i>	oval, slightly enlarged RBC, Schuffner's dots	schizonts present
<i>P. malariae</i>	normal-sized RBC	schizonts present

¹ Morphological characteristics are explained in the text and references 2-4.

Table 2. Chemoprophylaxis of malaria in adults^{1,2}

Drug	Prophylactic Regimen
Chloroquine	500 mg (salt) orally once a week starting 2 weeks before, while in the area, and 4 weeks after leaving malaria-endemic area.
Fansidar	3 tablets for presumptive treatment of malaria.
Doxycycline	100 mg/day orally starting 1-2 days before, while in the area, and 4 weeks after leaving malaria-endemic area.
Proguanil	200 mg/day orally in conjunction with weekly chloroquine.
Mefloquine	250 mg per week orally for first 4 weeks, then every other week. Prophylaxis should start 1 week before entering and 4 weeks after leaving.

¹ Adapted from reference 6

² Pediatric doses and up-to-date recommendations for individual countries can be found in reference 6 and the Traveler's Clinic of Rhode Island.

The normal adult dose is 500 mg (salt) once a week, starting two weeks before entering a malaria endemic area, the entire time while in the region and 4 weeks after leaving. Potential side effects include gastrointestinal upset and headache which are alleviated when the medication is taken with meals.

Current recommendations by the Center for Disease Control for chemoprophylaxis against chloroquine-resistant *P. falciparum* must be tailored to the individual and his travel plans (reference 6, Table 2). Chloroquine is still the mainstay of prophylaxis since this will protect the traveler against non-falciparum species as well as chloroquine-susceptible *P. falciparum* (still prevalent in chloroquine-resist-

ant areas). In addition, however, individuals should carry with them a single treatment course (3 tablets) of Fansidar® (pyrimethamine-sulfadoxine). If fever or flu-like symptoms develop, the traveler should rapidly seek medical attention. If medical care is not readily available, the traveler should take the three tablets of Fansidar at one time and then seek more definitive care as soon as possible. Travelers should be warned that Fansidar resistance has been noted in Thailand and Burma.

People who are allergic to sulfonilamide or pyrimethamine and short-term travelers (less than 3-4 weeks) to areas with extensive chloroquine and Fansidar-resistant malaria (Thailand, Burma) may elect to take doxycycline, but this is contraindicated for pregnant women, children under 8 years of age and may induce a photosensitivity reaction (like tetracycline) upon extensive sun exposure.

Proguanil (Paludrine®) is another anti-malarial drug available in Europe and Africa but not in the United States. Limited data suggests that it may be effective against chloroquine-resistant malaria in East Africa but not Thailand, Papua New Guinea or West Africa. Travelers using proguanil should take a daily 200 mg dose (adult) in combination with a weekly regimen of chloroquine.

Mefloquine (Lariam®) has been recently approved for the treatment and prevention of *P. falciparum* resistant to other anti-malarial drugs. It is recommended for travelers to areas where there is a risk of chloroquine-resistant *P. falciparum* infection, and by travelers to areas where *P. falciparum* is resistant to both chloroquine and Fansidar. Oral prophylaxis should start 1 week before visiting the area, continued while there and for 4

weeks upon leaving the malaria endemic area. The recommended dosage regimen is one 250 mg tablet weekly for the first 4 weeks then every other week. Minor side-effects include gastrointestinal distress and dizziness but these are self-limited. Because mefloquine has been occasionally associated with asymptomatic sinus bradycardia and a prolonged QT interval, it should not be used by individuals using beta-blockers, calcium channel antagonists or other drugs that alter cardiac conduction. Furthermore, mefloquine can alter blood levels of anti-convulsant drugs causing low anti-epileptic drug levels and breakthrough seizures.

Treatment

The choice of chemotherapeutic agents for malaria was at one time simple since all four parasite species were susceptible to chloroquine. However, in recent years, chloroquine-resistant *P. falciparum* malaria has emerged, being found in Southeast Asia, the Indian subcontinent, Oceania, Africa and South America.⁶

The choice of chemotherapeutic agents for malaria was at one time simple since all four parasite species were susceptible to chloroquine. However, in recent years, chloroquine-resistant P. falciparum malaria has emerged.

In the treatment of malaria, the physician must decide whether the patient has chloroquine-susceptible or -resistant malaria. If the patient is infected with *P. vivax*, *P. ovale*, *P. malariae*, or *P. falciparum* from an area where drug resistance has not developed (Haiti, the Dominican Re-

Table 3. Treatment guidelines for malaria in adults¹

Indication	Drug	Dose
<i>P. vivax</i> , <i>P. ovale</i> , <i>P. malariae</i> , chloroquine-sensitive, <i>P. falciparum</i>	Chloroquine	1 gram (salt) followed by 500 mg six hours later, than 500 mg per day for 2 days.
<i>P. falciparum</i>	Primaquine (for <i>P. vivax</i> and <i>P. ovale</i>)	26.3 mg salt p.o. per day for 14 days.
chloroquine-resistant malaria	quinine plus Fansidar	quinine 650 mg. p.o. every 8 hrs. for 3-10 days ² . Fansidar, 3 tablets p.o., single dose.
	quinine plus pyrimethamine and sulfadiazine	quinine as above; pyrimethamine 25 mg PO QID × 3 days; sulfadiazine 500 mg PO QID × 5 days
	Quinine plus tetracycline	quinine as above; tetracycline 250 mg po every 6 hrs for 7 days

¹ For pediatric doses, see reference 4.

² Longer treatment with quinine is preferred for treatment of individuals infected with *P. falciparum* from Southeast Asia. Consider mefloquine as an alternative drug.

public, Central America, Middle East), chloroquine is the drug of choice. If not, the patient should be treated with quinine and tetracycline. Alternate treatment would be quinine and Fansidar. Many physicians prefer tetracycline over Fansidar since resistance to the latter drug is found in South America, East Africa, and Southeast Asia. Furthermore, the extent of Fansidar resistance is rapidly spreading. The Traveler's Clinic at The Miriam Hospital recently saw a young man with *P. falciparum* malaria resistant to both chloroquine and presumably Fansidar. He obtained the infection in West Africa, an area not previously reported to have Fansidar resistance. If the physician is unsure whether the strain of *P. falciparum* is resistant to chloroquine or not, the patient should be treated with quinine and tetracycline.

Chloroquine-susceptible malaria (for adults) is treated with chloroquine orally 1 gram (salt) followed 6 hours later with 500 mg and then a single dose of 500 mg per day for 2 days (Table 3). To eradicate the dormant liver stages of *P. vivax* and *P. ovale* and thus prevent relapse, primaquine phosphate (15 mg base per

day orally for 14 days) should be given after completion of chloroquine treatment. Since primaquine can induce hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency, every individual should be screened for this deficiency prior to treatment.

All patients with chloroquine-resistant *P. falciparum* malaria should be hospitalized and treated immediately. One regimen is quinine sulfate 650 mg (adults) orally every 6 hours for 7 days (Table 3). Alternatively, quinine can also be given with a single administration of three tablets (adult) of Fansidar.

Quinine may be toxic, causing nausea, vomiting, headache, tinnitus, prolonged QT interval, and hypoglycemia. If the patient is unable to take quinine orally, a parenteral form can be given but must be obtained from the Centers for Disease Control. Recent studies have found quinidine gluconate to be as effective as quinine, but since quinidine can cause hypotension or cardiac arrhythmias, all individuals should be closely monitored in an intensive care unit.

Treatment of individuals infected with malaria from South-

Malarial infection is more severe in pregnant women than in nonpregnant women. Furthermore, the incidence of prematurity, spontaneous abortion and still-birth is increased in women infected with malaria.

east Asia is difficult because of the widespread development of resistance to many chemotherapeutic agents. Mefloquine, in combination with either Fansidar or quinine, provides another therapeutic option. Advice of tropical disease specialists should be sought in this instance.

Pregnant Women

Malarial infection is more severe in pregnant women than in nonpregnant women. Furthermore, the incidence of prematurity, spontaneous abortion and still-birth is increased in women infected with malaria. Pregnancy is not a contraindication to prophylaxis with chloroquine since the drug has not been found to have any harmful effects on the fetus. However, other drugs used to prevent infection with chloroquine-resistant malaria are not consid-

ered safe in pregnancy. The best advice for a pregnant woman who contemplates traveling to an area with chloroquine-resistant malaria is to stay home.

Further Information

Recommendations on malaria prophylaxis, and the countries where chloroquine-resistant *P. falciparum* is found, are constantly changing. Relatively recent information can be found in "Health Information for International Travel" 1989 (HHS Publication No. 89-8280) or is available at either the Traveler's Clinic at the Miriam Hospital (401-274-3700) or The Memorial Hospital (401-722-6000).

References

- 1 Kean BH, Reilly PC. (1976) "Malaria — The Mime." Am. J. Med., 61:159-164.
- 2 Miller LH, "Malaria" in Tropical and Geographic Medicine" Eds. KS Waren and AAF Mahmoud. McGraw-Hill, New York (1984).
- 3 Manson-Bahr PEC and DR Bell "Manson's Tropical Diseases." Nineteenth Edition. Bailliere, Tindall, London (1987).
- 4 Wyler DJ. "Plasmodium species (Malaria)" in Principles and Practices of Infectious Diseases." (1989) Eds. Mandell GL, Douglas RG, Bennett TE, Churchill Livingstone, New York, 1989.
- 5 Warrell DA, Loovareesuwat S, Warrell MJ, Kasemsam P, Intaraprasert R, Buunag D, Harinasuta T. (1982). "Dexamethasone proves deleterious in cerebral malaria." NEJM 306:313-319.
- 6 Health Information for International Travel, 1989. US Department of Health and Public Services (HHS Publication No. 89-8280), US Government Printing Office, Washington, DC.
- 7 Miller KD, Greenburg AE, Campbell CC (1989). "Treatment of severe malaria in the United States with a continuous infusion of quinidine gluconate and exchange transfusion." NEJM 321:65-70.
- 8 Krogstad DJ and Herwaldt BL. (1988). "Chemoprophylaxis and treatment of malaria." NEJM 319:1538-1540.

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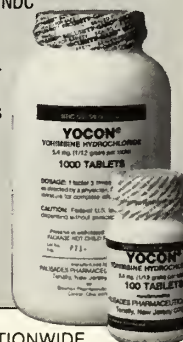
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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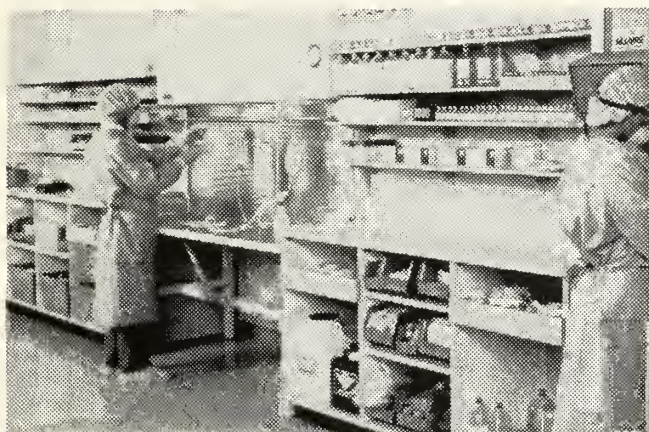
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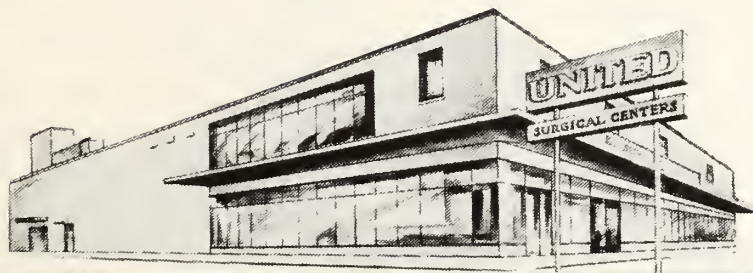
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Comparison of Laboratory Test Use Among Three Urgent Care Clinics

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The present study compares laboratory test usage among doctors practicing at fee-for-service units and HMOs, where health care is prepaid.

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Recently, a number of "walk-in" or "urgent care" clinics have sprouted, some associated with health maintenance organizations (HMOs) or medical centers and others independent or free-standing. A recent *New England Journal of Medicine* report presents a personal account of a physician working in the "brave new world" of medicine — a walk-in clinic.¹ The paper discusses issues regarding administrative policies and incentives governing the use of laboratory tests. The present study compares laboratory test usage, among doctors practicing at fee-for-service units and HMOs, where health care is prepaid. We selected three settings in southeastern New England for study.

Methods

The three clinics are within a 30-mile radius of Brown University, Providence, Rhode Island. One urgent care facility functions within a large and successful HMO. The HMO encourages clients to call by phone first and has a clinician available to prescribe home care instead of an office visit if that is appropriate. A second facility is a physician-owned fee-for-service walk-in clinic at a shopping mall. And the third is a fee-for-service walk-in clinic that is part of a larger physician-owned multi-specialty

group practice. Permission was obtained to review the medical records of recent patients (1988) with either of two medical problems: cough (upper respiratory infection) or diarrhea. All cases accepted for study were first visit presentations; repeat visits were excluded. Because only one facility included pediatric patients, and another excluded Medicare patients, patients under the age of 19 and over the age of 60 were excluded.

Using a standard protocol, the following information was abstracted: patient's age, sex, chief complaint, duration of illness and laboratory tests ordered (Table 1). The data were entered into an Apple Macintosh computer and analyzed with a STAT 513 program. The X^2 test (or Fisher's exact test where applicable) was used to compare categorical data and the student t test was used to compare means among sites (in every case, one site was compared to the two others).

Results

Two hundred and twenty-one (221) cases were available for study and are presented in Table

ABBREVIATIONS USED:

HMO: Health Maintenance Organization

SD: Standard deviation

**Table 1. Laboratory Tests
Tabulated at Three Sites**

Complete Blood Count
Chest Radiograph
Throat Culture
Blood Culture
Sinus Radiograph
Pulmonary Function Tests
Sputum (Gram Stain)
Abdominal Radiograph
Stool Culture
Abdominal Ultrasound
Stool Occult Blood
Fecal Ova and Parasites
Serum Electrolytes
Urinalysis
Electrocardiogram
Erythrocyte Sedimentation Rate
Serum Chemistry 12
Serum Chemistry 24
Others
Total Number of Laboratory Tests Ordered

2. The three patient groups studied were approximately similar in age and sex distribution, and duration of illness.

The chief complaint of cough or upper respiratory infection occurred two to four times more frequently than diarrhea. Laboratory tests most frequently used to aid the diagnosis of cough or upper respiratory infection are summarized in Table 3. The free-standing walk-in clinic ordered significantly more throat cultures than the other two sites, and averaged almost twice as many tests per visit as the HMO. The HMO ordered sinus radiographs and throat cultures significantly less frequently than the other two sites.

Laboratory tests most frequently used to aid in the diagnosis of diarrhea are summarized in Table 4. The free-standing walk-in clinic ordered more serum chemistries than the other two sites. The walk-in clinic at a medical center ordered more stool cultures and more stool smears for fecal leukocytes than the other two sites. The walk-in clinic at a medical center ordered the most tests per patient work-up (3.8), and the HMO ordered the least

(2.1), but the differences were not statistically significant.

When work-ups for both diagnoses were considered together, the free-standing walk-in clinic made the most extensive use of laboratory tests, the HMO used them least often, and the walk-in clinic at a medical center made an intermediate use of the laboratory.

Discussion

The results indicate that physicians working at a free-standing walk-in clinic order significantly more tests than those working at an HMO or in the walk-in component of a private, fee-for-service group practice. In instances of specific test use (ie, throat culture or sinus x-ray), the HMO ordered significantly fewer tests than the other two sites; and while overall test use is not significantly lower at the HMO, compared with the two fee-for-service sites, test use is significantly higher at the free-standing walk-in clinic compared with the two other sites. The three patient populations studied are similar, thus validating comparisons of laboratory test use to evaluate patients with upper respiratory infection or diarrhea. The fact that the duration of illness was longer prior to the visit for HMO patients is surprising, because no fiscal barriers prevent HMO patients from seeking earlier care. This observation may indicate that earlier care does not reduce test use, however, this finding is difficult to interpret because HMO patients had access to the facility by telephone.

The finding that physicians who practice in HMOs order fewer tests is supported by prior studies revealing that the care provided by HMOs costs 10 percent to 40 percent less than that provided to comparable populations who use the fee-for-service system.² There is good evidence that the quality

of care rendered by prepaid groups is equal to that provided by fee-for-service practices.³ Financial incentives may be an important factor in explaining the cost differences between prepaid and fee-for-service care. This is further suggested by published comparisons of test-ordering behavior in ambulatory care settings among British and American physicians, with the latter making more use of the laboratory in their usual practice.⁴

When work-ups for both diagnoses were considered together, the free-standing walk-in clinic made the most extensive use of laboratory tests, the HMO used them least often, and the walk-in clinic at a medical center made an intermediate use of the laboratory.

However, the fiscal or reimbursement structure of the practice setting is far from being the only or decisive factor in determining test use by physicians. For example, family practitioners order fewer tests than internists.⁵ Physicians, members of large group practices, order twice as many tests for their hypertensive patients as physicians in small groups or in solo practice.⁶ Recent graduates from medical school are heavier users of the laboratory than more senior physicians.⁶ In addition to individual physician characteristics, the setting in which doctors practice appears to have some influence in determining test use. For example, physicians who care for terminal cancer patients in a hospice setting order fewer tests⁷ and fewer treatments⁸ than physicians who care for the same types of patients in a hospital setting. A major difficulty in explaining dif-

Table 2. - Comparison of Case Material Among Clinics

	Urgent Care at HMO		Walk-in at Medical Center		Free- standing Walk-in Clinic		Total	
	n	%	n	%	n	%	n	%
<i>Total Cases (Ages 19-60) Reviewed</i>	78		72		71		221	
Sex:								
Males	30	(38)	27	(38)	22	(31)	79	(36)
Females	47*	(60)	45	(63)	48*	(68)	140	(63)
Age:								
19-25	21	(27)	19	(26)	18	(25)	58	(26)
26-35	27	(35)	19	(26)	24	(34)	70	(32)
36-45	19	(24)	17	(24)	15	(21)	51	(23)
46-55	09	(12)	12	(17)	11	(15)	32	(14)
56-60	02	(03)	05	(07)	03	(04)	10	(05)
All subjects mean age \pm SD	34.0 \pm 10.30		36.2 \pm 11.9		34.3 \pm 11.03		34.8 \pm 11.1	
Chief Complaint:								
Cough	54	(69)	58	(81)	57	(80)	169	(76)
Diarrhea	24	(31)	14	(19)	14	(20)	52	(24)
Mean duration of illness (days)	9.75 \pm 22.3**		8.06 \pm 9.0		7.1 \pm 6.9		8.4 \pm 14.7	
Geometric Mean duration of illness	4.85		4.8		4.7		4.8	

* In two instances sex was unavailable.

** One patient had been coughing for 180 days; when excluded, the mean duration of illness at the HMO was 9 days.

Table 3. Tests Used to Aid the Diagnosis of Upper Respiratory Infections

	Urgent Care at HMO		Walk-in at Medical Center		Free-standing Walk-in Clinic		Total	
	n	%	n	%	n	%	n	%
<i>Number of Patients Reviewed</i>	54		58		57		169	
<i>Tests Most Frequently Ordered:</i>								
1) Chest Radiograph	21	(39)	24	(41)	25	(44)	70	(41.4)
2) Throat Culture	07	(13)**	12	(21)	32	(56)****	51	(30.2)
3) Complete Blood Count	11	(20)	08	(14)	15	(26)	34	(20.1)
4) Sinus Radiograph	03	(06)**	14	(24)	12	(21)	29	(17.2)
5) Serum Chemistry 12	01	(02)	05	(09)	06	(10)	12	(07.1)
Average Number of Tests/Patient ¹ \pm SD	1.0 \pm 1.15		1.21 \pm 1.20		1.95 \pm 1.37****		1.39 \pm 1.30	

¹Includes other tests listed in Table 1.

** p < 0.01

*** p < 0.001

**** p < 0.0001

Table 4. Tests Used to Aid the Diagnosis of Diarrhea

	Urgent Care at HMO		Walk-in at Medical Center		Free-standing Walk-in Clinic		Total	
	n	%	n	%	n	%	n	%
<i>Number of Patients Reviewed</i>	24		14		14		52	
<i>Tests Most Frequently Ordered:</i>								
1) Complete Blood Count	12	(50)	10	(71)	11	(79)	33	(63.4)
2) Serum Chemistry 12	02	(08)**	05	(36)	09	(64)**	16	(30.8)
3) Urinalysis	07	(29)	05	(36)	04	(29)	16	(30.8)
4) Stool Culture	03	(12)	07	(50)*	03	(21)	13	(25.0)
5) Stool Occult Blood	04	(17)	05	(36)	01	(07)	10	(19.2)
6) Fecal Leukocytes	01	(04)	05	(36)*	02	(14)	08	(15.4)
Average Number of Tests/Patient ¹ \pm SD	2.12 \pm 2.42		3.8 \pm 3.26		2.93 \pm 2.13		2.79 \pm 2.65	
	SE 0.49		SE 0.87		SE 0.57		(0.367 SE)	

¹ Includes other tests listed in Table 1.

* p < 0.05

** p < 0.01

ferences in test use is related to the self-selection of physicians and patients alike into particular practice settings and reimbursement systems. In all likelihood, patient preferences, physician characteristics, the nature of the setting of care and the mode of

Reasons for testing . . . include screening, diagnosis, prognosis, monitoring treatments, baseline information, reassurance, patient expectations, physician education, fear of litigation.

payment interact in some complex fashion to determine how medical care (including test use) is rendered.

Reasons for testing have been listed in many papers^{9,10} and include screening, diagnosis, prognosis, monitoring treatments, baseline information, reassurance, patient expectations, physician education, fear of litigation, etc. The present study, which focuses specifically on diagnostic tests used for simple and common ambulatory problems, indicates that the setting of care may influence test use either directly by pressuring physicians to order more or fewer tests, or indirectly by attracting patients, physicians and payers who in some interactive way make more or less use of laboratory tests. The setting of care, however, regardless of the mechanism, is an important determinant of test use. The health policy implication is obvious if one can assume equal outcome of care: cost-effective settings should be promoted by the planners, regulators, and payers of health care.

Summary

Laboratory test ordering practices among physicians at three walk-in or urgent-care medical facilities

were compared to evaluate the relationship between practice type and test ordering patterns. The charts of 221 patients were reviewed for test ordering as an aid for the diagnosis of cough or upper respiratory infection (169 patients) or diarrhea (52 patients). For upper respiratory infections, the free-standing walk-in clinic ordered the greatest number of tests; and for both categories of disease, the urgent care unit of a health maintenance organization (HMO) ordered the fewest tests.

References

- 1 Bock RS: The pressure to keep prices high at a walk-in clinic: A personal experience. *N Engl J Med* 1988;319:785-787.
- 2 Luft HS: How do health maintenance organizations achieve their "savings." *N Engl J Med* 1978;298:1336-1343.
- 3 Manning WG, Leibowitz A, Goldberg GA, et al: A controlled trial of the effect of a prepaid group practice on use of services. *N Engl J Med* 1984;310:1505-1510.
- 4 Hartley RM, Epstein AM, Harris CM, McNeil BJ: Differences in ambulatory test ordering in England and America. Role of doctors' beliefs and attitudes. *Am J Med* 1987;82:513-517.
- 5 Bertakis KD, Robbin JA: Gatekeeping in primary care: A comparison of internal medicine and family practice. *J Family Practice* 1987;24:305-309.
- 6 Epstein AM, McNeil BJ: Physician characteristics and organizational factors influencing use of ambulatory testing. *Med Decision Making* 1985;5:401-415.
- 7 Wachtel TJ, Mor V: Physicians use of health resources for terminal cancer patients: Clinical setting versus physician specialty. *Southern Med J* 1987;80:1120-1124.
- 8 Wachtel TJ, Mor V: The use of transfusion in terminal cancer patients. Hospice versus conventional care setting. *Transfusion* 1985;25:278-279.
- 9 Lundberg GDL: Perseveration of laboratory test ordering: A syndrome affecting physicians. *JAMA* 1983 249:639.
- 10 Griner PF, Glaser RJ: Misuse of laboratory tests and diagnostic procedures. *N Engl J Med* 1982;307:1336-1339.

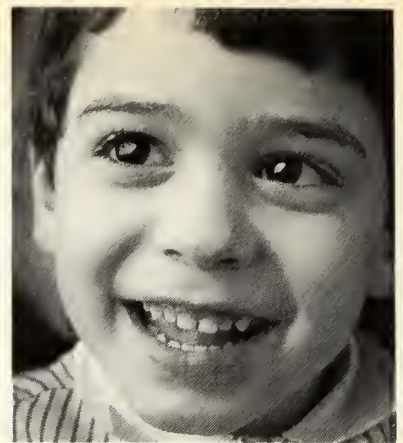


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Axid does not inhibit the cytochrome
P-450 metabolizing enzyme system.²*

Swift and effective H₂-antagonist therapy

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rapidly and effectively^{4,5}*
- *Dosage for adults with active
duodenal ulcer is 300 mg once nightly
(150 mg b.i.d. is also available)*

References

1. *USP DI Update*, September/October 1988, p 120.
2. *Br J Clin Pharmacol* 1985;20:710-713.
3. Data on file, Lilly Research Laboratories.
4. *Scand J Gastroenterol* 1987;22(suppl 136):61-70.
5. *Am J Gastroenterol* 1989;84:769-774.

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Brief Summary. Consult the package literature for complete information.

Indications and Usage: 1. *Active duodenal ulcer*—for up to eight weeks of treatment. Most patients heal within four weeks.

2. *Maintenance therapy*—for healed duodenal ulcer patients at a reduced dosage of 150 mg h.s. The consequences of therapy with Axid for longer than one year are not known.

Contraindication: Known hypersensitivity to the drug. Use with caution in patients with hypersensitivity to other H₂-receptor antagonists.

Precautions: *General*—1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests—False-positive tests for urobilinogen with Multistix[®] may occur during therapy.

Drug Interactions—No interactions have been observed with theophylline, chloridazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system, therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect; but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported. **Endocrine**—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

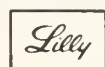
Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdose occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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Additional information available to the profession on request.



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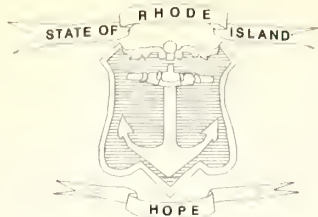
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HEALTH BY NUMBERS

Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

Malaria In Rhode Island

Fifty-two cases of malaria were reported to the Rhode Island Department of Health, Division of Disease Control, during the six-year period 1984-1989. Two cases have been reported so far in 1990. Nineteen cases were reported in 1989, a dramatic increase from the annual total of four to eight cases reported in each of the previous five years (Figure 1). One patient died of malaria in 1989, the only death in the six-year period.

Overall, two-thirds of case-patients were male and one-third female. Most case-patients were young adults between 20 and 45 years of age. More than half of all patients, and three quarters of the 1989 cases, were United States citizens exposed while traveling or working in endemic areas (Table 1). One-quarter of case-patients were white and the majority of the non-white patients were black. Only ten percent of case-patients were Asian and fewer were Hispanic.

The malaria species was specified in almost 90 percent of the case reports. The predominant species were *Plasmodium vivax* and *P. falciparum* and each accounted for almost half the total cases

reported. Less than 5 percent of case-patients were infected with *P. malariae* or *P. ovale* (Table 2).

Our experience differs from that reported nationally by the Centers for Disease Control in several important ways. The reported incidence rate of malaria in Rhode Island on average is about double the national rate and was four times the national rate in 1989. A greater proportion of Rhode Island malaria cases have occurred in American citizens and the proportion of our cases with *P. falciparum* infection is nearly double the 26 percent to 29 percent reported nationally.

The dramatic increase in Rhode Island cases in 1989 did not represent a defined outbreak. Cases were not associated with travel to any single country or with patient's race, ethnic background or national origin.

All Rhode Island physicians should remember that they may see patients with malaria in their own practices. Many Rhode Islanders travel for business, pleasure, or education to parts of the world where malaria is endemic. Careful attention to proper counseling about ma-

laria prophylaxis before travel will help prevent the disease in travelers. Correct diagnosis of malaria depends on eliciting a travel history and including malaria in the differential diagnosis of suggestive illnesses. Laboratory confirmation requires careful evaluation of thick and thin blood films by an experienced technologist. Repeated tests may be necessary.

Malaria remains a common and deadly disease in much of the world. It may seem remote and exotic to American physicians but we need to help prevent malaria and be prepared to recognize it in our patients.

Figure 1. Reported Cases of Malaria, Rhode Island, 1984-1989

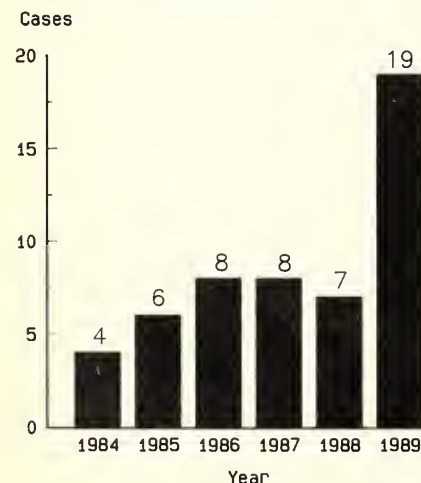


Table 1. Distribution of Malaria Cases by Citizenship Category, Rhode Island, 1984-1989

Species	Cases	Percent
<i>P. Vivax</i>	19	37
<i>P. Falciparum</i>	22	42
<i>P. Malariae</i>	3	6
<i>P. Ovale</i>	2	4
Not Determined	6	11

Table 2. Distribution of Malaria Cases by *Plasmodium* Species, Rhode Island, 1984-1989

	Cases	Percent
US Civilian	29	56
Foreigner	21	40
US Military	1	2
Unknown	1	2

Submitted by the Division of Disease control, Thomas T. Gilbert, MD, Acting Medical Director. *Health by Numbers* is edited by Jay S. Buechner, PhD, and William J. Waters, Jr., PhD.

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with January 1990	
	January 1990 Number	Number	Rates
Live Births	1,067	15,330	15.4*
Deaths	929	9,777	9.8*
Infant deaths	(13)	(158)	10.3†
Neonatal deaths	(11)	(127)	8.3†
Marriages	246	8,267	8.3*
Divorces	376	3,680	3.7*
Induced Terminations	714	7,936	517.7†
Spontaneous Fetal Deaths	42	1,121	73.1†
Under 20 weeks' gestation	(35)	(1,003)	65.4†
20+ weeks' gestation	(7)	(107)	7.0†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with October 1989		
	October 1989 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	292	3,452	347.6	4,692.0
Malignant Neoplasms	231	2,462	247.9	7,367.0
Cerebrovascular Diseases	46	607	61.1	1,083.5
Injuries (Accident, Suicide, Homicide)	36	434	43.7	9,963.0
COPD	36	301	30.3	441.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

PHYSICIANS IN THE NEWS

Dr Richard G. Bertini, Orthopedist-in-Chief at Memorial Hospital, was recently elected to the Board of Trustees of Talladega College, Alabama.

* * *

Dr David G. Kern, Director of General Internal Medicine at Memorial and Director of Brown University's Program in Occupational Medicine, has been appointed to the Selection Committee of the Association of Occupational and Environmental Clinics. **Dr Kern** was also appointed to the Advisory Boards of the Harvard Educational Resource Center, the Harvard/University of Massachusetts Occupational Medicine Residency, the New England Consortium on Health and Safety Training for Hazardous Waste Workers, and the Brown University Department of Medicine Curriculum Committee.

* * *

Recent appointments to the Medical Staff at St Joseph Hospital include: **Dr George M. Hanna**, Division of Internal Medicine; **Dr Cynthia M. Hanna**, Department of Obstetrics/Gynecology; **Dr Michael P. Mariorenzi**, Division of Orthopedics; **Dr David Garson**, Division of Gastroenterology.

* * *

The following department chairmen were recently elected at Newport Hospital: **Dr James C. Gedney**, Chairman of the Department of Obstetrics and Gynecology; **Dr Richard R. Knowles**,

Chairman of the Department of Medicine; **Dr George P. Lewis, Jr.**, Chairman of the Department of Surgery; **Dr Kenneth B. Stern**, Chairman of the Department of Psychiatry. Medical Staff Officers include: **Dr Charles P. Shoemaker, Jr.**, President; **Dr Edwin G. Singsen**, President-Elect; **Dr Arthur A. Frazzano**, Secretary-Treasurer.

* * *

Dr Patrick Dowling, director of the Family Residency Program at Memorial Hospital, was presented with the Regional Health Administrator's Award from the US Public Health Service. The award is given to those who have made an outstanding contribution in the field of public health in New England. **Dr Dowling** was recognized for implementation of the Community Health Center Model which trains family practice residents in Rhode Island.

* * *

A third-year resident in Internal Medicine at Memorial Hospital, **Dr Graca Does** was recently nominated to present one of eight abstracts at the National Meeting of the American College of Physicians. The paper, "Endothelium, von Willebrand Factor, and Atherosclerosis" was presented in Chicago in April.

* * *

Dr Mark S. Weinberg is principal investigator of a blood pressure research study on Doxazosin, awarded by Roerig division. He is also Chairman of the Work-

site Committee, American Heart Association, Rhode Island Affiliate.



SPEAK UP AMERICA

Whenever medicines are prescribed, tell your health professionals:

1. the medicines you are taking, including nonprescription medicines;
2. any problems you are having with your medicines;
3. medicines to which you are allergic;
4. if you are, or think you might be, pregnant.



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PATIENT
INFORMATION AND
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THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME 1
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (May, 1940)

The *Journal* prints the annual address of the president of the Pawtucket Medical Association, Thad A. Krolicki, MD.

The lead scientific article is authored by Bertram H. Buxton, MD and discusses the management of obstetrical hemorrhage. It is a detailed inquiry into the causes of bleeding and the available therapeutic interventions throughout the various trimesters of pregnancy as well as during the intrapartum and postpartum periods. The author summarizes his observations by emphasizing: "1.

The importance of asepsis in the treatment of miscarriages remembering that these cases die of sepsis rather than hemorrhage. Also, not to curet septic cases until the temperature has remained normal for several days. 2. Miscarriage in the second trimester should be treated as premature labor. Do not attempt to dilate and remove foetus through undilated cervix. 3. Bleeding in the third trimester should be regarded with respect and before examination is made, every preparation made to cope with any emergency that may arise at the time of examination. These cases should all preferably be sent to the hospital for examination. 4. The importance of transfusion in saving

these cases should be recognized and the importance of having patients typed and donors procured before the emergency arises.

5. The danger of rupture of the uterus in improper use of Pituitrin and inadvisable operative manoeuvre through an undilated cervix. 6. The management of the third stage of labor with regard to not hastening separation of the placenta and in watchful care of patients for one hour postpartum. 7. The increasing danger of sepsis associated with the decrease in the resistance of the patient in all these hemorrhage cases."

A brief editorial is printed concerning army experience for physicians. The editorial states the following: "Physicians under thirty-five years of age who are desirous of obtaining extended active duty with the Army but who do not hold Reserve commissions are being offered appointments in the Medical Corps Reserve in the grade of 1st Lieutenant, in order to permit them to be placed on such duty." The article further states: "The pay and allowances for a married 1st Lieutenant amount to approximately \$263.00 a month. . . . Application for one year of active duty, or for appointment in the Medical Corps Reserve with a view

to obtaining one year of active duty with the Army, should be requested at once by a letter addressed to the Commanding General of the Corps Area wherein the physician permanently resides." (*Edit. Note: The time is May in the year 1940. The United States is not at war but the German armies in the west have already subdued Denmark, Norway, Belgium and the Netherlands, have entered Paris and have reached the English Channel. The Japanese attack upon Pearl Harbor will not occur for another 19 months.*)

Another editorial notes that May 12 is the anniversary of the birth, in 1820, of Florence Nightingale and is set apart, now, as National Hospital Day.

Various recently acquired medical texts are reviewed. The 1939 Yearbook of General Medicine is discussed as a worthy collection of abstracts covering the major subspecialties of internal medicine. The illustrated text is over 800 pages in length and the hardcover edition sells for three dollars.

* * *

Twenty-Five Years Ago (May, 1965)

William B. Kannel, MD, Associate

Director of the Heart Disease Epidemiology Study in Framingham, Massachusetts, writes a comprehensive article entitled, Comparison of Serum Lipids in the Pre-dissection of Coronary Heart Disease.

He observes: "Thus, since no "safe levels" of cholesterol have been identified in this population, and a gradient of risk is observed from the lowest to the highest levels, judgment as to when to become concerned must depend very much on the presence or absence of these other factors. Using ordinary office procedure, the physician can identify coronary prone individuals and estimate the magnitude of the risk they run. This can be done many years before the onset of overt disease, hopefully in time to institute effective preventive measures."

"The need for a preventive approach in this disease is the chief lesson learned from study of the natural history of the disease. Prevention and not further innovations in treatment will be required if a significant reduction in morbidity and mortality from this disease is to be achieved. The critical period in a heart attack appears to be the first few minutes. Approximately 55 percent of all the deaths, in the acute phase (first three weeks), occurred in these first few minutes after the onset of the attack. In about 65 percent of these sudden deaths there was no overt preceding hint of impending disaster. The overall case fatality rate in the acute stage in subjects having a "heart attack" was an appalling 35 percent. In spite of impressive innovations in diagnosis and treatment over the past century, the case fatality rate in this disease has not been substantially reduced because of the occurrence of sudden unexpected death in apparently well individuals. The

importance of coronary heart disease as a cause of death and disability is so widely recognized that it hardly needs emphasis. In Framingham, where 5,127 men and women aged 30-60 years have been followed for more than twelve years, one in every 20 women and one in every ten men have developed this disease in the period of observation. . . . An attitude towards disease similar to that taken by the pediatrician or the obstetrician, in which preventive maintenance is given top priority, will be required if inroads are to be made against this number one killer in the USA. In the development of a preventive approach to this disease, the serum lipids will play a dominant role in identifying the highly susceptible individual for whom an effective program of prevention is imperative."

Drs Gerhard Meier and Ahmed Mohiuddin of Newport Hospital describe a 23-year-old female who was admitted to the hospital because of cough, fever, easy bruising and nose bleed. A large spleen was noted. The WBC count was 131,000 with 60.5 percent neutrophils and a diagnosis of subacute myelogenous leukemia was made. Radiation therapy was undertaken. About 11 months after the diagnosis was made, the patient was delivered of a healthy fullterm male baby. A year later, the patient's WBC count was 132,400. The authors discuss the concurrence of leukemia and pregnancy, noting that only 140 such cases are reported in the literature.

The lead editorial comments on various contemporary studies attempting to identify the coronary heart disease prone patient. Many of the studies conclude that such a patient is older, shorter, more mesomorphic, has higher values for serum cholesterol, uric acid and phospholipids, and is more

likely to have a father and mother with proven coronary heart disease.

Another editorial discusses the problem of medical student attrition and the attitudes of current medical educators: "If every medical school in the United States each year salvaged but a single student now lost to the profession through attrition, the total would be the equivalent of an entire graduating class of almost one hundred students. In terms of economics, considering the costly process of building and staffing new medical schools, the problem is worthy of attention." The editorial concludes by noting that we should not be dismayed if a few of our profession do not practice medicine. Erasmus, Rabelais, Oliver Goldsmith, Cronin and Somerset Maugham have enriched our lives and they "attest to the value of a medical education for a deeper understanding of the perplexities and meanings of life."

The officers of the Rhode Island Medical Society for the year are: William A. Reid, President; Walter J. Dufresne, Vice President; Harry E. Darrah, President-elect; Michael DiMaio, Secretary; John A. Dillon, Treasurer; Arthur E. Hardy, AMA delegate; and Seebert J. Goldowsky, Editor-in-Chief of the *RI Medical Journal*.

UNDERSTANDING CME

Edited by
Kimberly Allyn,
RIMS CME Coordinator

Janice Miller, M.Ed.,
Director,
Office of CME
Brown University

Category 1 & Category 2

There are two categories of continuing medical education, Category 1 & Category 2. As defined by the American Medical Association, a Category 1 CME activity must be "sponsored or co-sponsored by an organization accredited for continuing medical education by one of the state medical societies or by the Accreditation Council for Continuing Medical Education (ACCME) and designated as Category 1 by that organization." Further, the activity must be "based on needs assessment, define clear objectives, use methods and content appropriate to the objectives, include evaluations, and document physician participation." These requirements encompass Essentials #2-#6 as developed by ACCME.

Category 2 educational activities can be provided by either an accredited or an unaccredited organization. No designation statements concerning category or amount of credit are used in program brochures for Category 2 activities.

Physicians self-report Category 2 activities for the Physician's Recognition Award (PRA) if they find that the activities meet the definition of CME and fulfill an

educational need. Category 2 activities include:

a) CME lectures and seminars not designated Category 1.

The fact that a program is not designated AMA/PRA Category 1 does not indicate that it is of poor quality, but only that it does not meet all of the educational requirements established for AMA/PRA Category 1 programs.

b) Medical teaching

c) Articles, publications, books, and exhibits

d) Non-supervised individual CME (self-instruction, consultation, patient care review, self-assessment)

e) Other meritorious learning experiences

The PRA was established by the American Medical Association (AMA) in 1968 to encourage physician participation in continuing medical education (CME) and to recognize physicians who have voluntarily completed programs of CME.¹ The AMA has supported the idea that all physicians should participate in CME throughout their careers. Approximately one half of all states require evidence that a physician has completed a minimum amount of CME to satisfy their requirements for state licensure.

Questions about Category 1 or Category 2 should be referred to

the organization sponsoring the CME activity. The Director of Medical Education (DME) of an accredited organization or the person responsible for the CME program should determine category approval of a CME activity.

* * *

ESSENTIAL #1 MISSION STATEMENT

The sponsor shall have a written statement of its continuing medical education mission, formally approved by its governing body. The mission statement shall:

1) *Describe the goals of the overall CME program in a concise manner.*

Why have a CME program?

- quality patient care
- new knowledge, skills
- refresh basic sciences
- CME credit required for licensure

2) *Indicate the scope of the CME effort.*

What type of activities are included in your program?

3) *Outline the characteristics of the potential participants.*

Who is the population that you serve?

4) Describe the general types of activities and services provided.

What type of CME services do you provide?

The mission statement should answer the questions "why, what, who, and how" in relation to the organization's CME program and be supported by the governing body. Periodic review and evaluation of the mission statement is necessary in determining whether it reflects the overall CME program and if changes are required.

ESSENTIAL #2 NEEDS ASSESSMENT

The sponsor shall have established procedures for identifying and analyzing continuing medical educational needs and interests of prospective participants. The sponsor shall:

1) Document the processes used to identify CME needs, including data sources which go beyond the sponsor's own perception of need.

2) State the overall needs identified by the above processes and indicate how this assessment is used in planning education activities.

Needs Assessment is the systematic procedure used by those involved in CME program planning to identify areas of knowledge or skills physicians should or wish to acquire, develop, or strengthen. The goal, then, in designing an educational program that meets the identified need, is to improve competency in medical practice.

A variety of needs assessment techniques may be used to determine areas in which physician competency can be enhanced and interest met. These include: a survey of prospective participants, patient care evaluation studies

such as quality assurance, chart review, and Morbidity/Mortality reports, informal suggestions, or new advances in knowledge, techniques, and equipment.

The following questions may be considered in determining which topics would be most relevant for your CME program:

1) How long has it been since the topic was last used for a CME session?

2) How many different assessment techniques indicated the need for the topic?

3) How likely is it that an educational session related to the need will benefit practice behavior?

4) How attractive will the topic be to the medical staff?

5) How available are the resources needed to put on an educational session on the topic?

6) How much will the unfulfilled need hinder health care delivery?

Needs assessment techniques used as well as identified needs can be recorded in Committee minutes or on worksheets used for planning the activities. Documentation provides a record that Essential #2 is being followed, can be used to refer back to as a measure of evaluating change in physician behavior, and is an important organizational element of the CME program.

References

¹ "The Physician's Recognition Award" published by the Office of Physician Credentials and Qualifications, American Medical Association, Chicago, Illinois.

Coming Up:

Essential #3 and #4

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For more information: Department of Education, American Academy of Pediatrics, 1-800-433-9016, ext. 7657

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For more information: Beth Paulsen, 1-800-274-2237, ext. 4220

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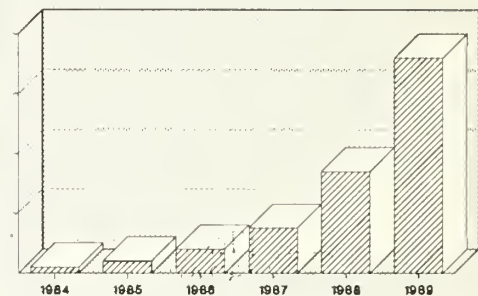


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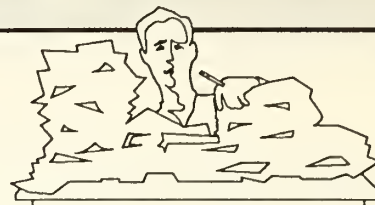
Cover: The leaves of the *Erythroxylon Coca* shrub from which cocaine is derived. Illustration by John LaRiviere.

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EDITORIALS

The Leaves of *Erythroxylon Coca*

In the 1950s a major television show was called "Coke Time" and everyone knew then that the title referred to a carbonated drink. Times have changed. Even today's children recognize that words such as "coke" and "snow" carry several meanings — one of them being cocaine.

Since pre-Columbian times, indigenous Andean cultures have adopted coca leaves, the only source of cocaine, for religious and social purposes. Chewing the leaves generated for them a sense of euphoric well-being; and in higher altitudes made their heavy manual labors seem less burdensome. Today, in much of rural Peru, Bolivia, Ecuador and Colombia, the majority of adults regularly chew coca leaves.

Discovery of the Americas yielded immense material wealth to the colonial empires of Europe, not the least of which was an abundance of botanical species hitherto unknown to the Eastern hemisphere. Some of these botanical discoveries included plants, such as quinine and coca leaves, which were of substantial medicinal value. Coca and its stimulant effects were first documented by Europeans in 1528 during Francisco Pizarro's conquest of Peru.

The botanist Jussieu sent coca specimens back to Paris in 1749 for purposes of botanical classification. Because of its reddish wood, Linnaeus and others placed the coca shrub in the genus *Erythroxylon*. Until this century it was believed that only one pharmacologically important species of

Erythroxylon coca existed but more recent morphologic studies by Plowman and others determined that there are two major cocaine-producing species, each with two cultivated varieties.¹ *E. coca* var. Huanuco (Bolivian coca) is a perennial shrub, both cultivated and feral, some 2 meters in height, which grows at elevations between 500 and 1,500 meters along the moist eastern slopes of the Andes in Ecuador, Peru and Bolivia. It is this variety which provides the bulk of the world's supply of cocaine. *E. coca* var. Ipadu (Amazonian coca) is locally harvested in the western reaches of the Amazon basin, has less commercial value and contains a lower leaf-concentration of psycho-active alkaloids. *E. novogranatense* var. Truxillense (Trujillo coca) is cultivated in the high, isolated valleys of northern Peru and can survive drought or low rainfall more readily than *E. coca*. Finally, *E. novogranatense* (Colombian coca) grows in the Andean valleys of Colombia and along the Caribbean coastal plain; it is better adapted to arid conditions, but has minor value as a commercial crop. All varieties of *Erythroxylon* require a mineral-rich, clay-like soil, low in lime content. The shrub, which yields as many as five crops of leaves per year, does not tolerate temperatures much below 18° C. The name coca, incidentally, is derived from the Inca word, *khoka*, meaning tree.

In Europe, coca leaves confined themselves to the pages of botanical texts until German

chemists attempted to distill the substance (thought initially to be caffeine) responsible for their stimulant effects. These efforts achieved success in 1859 when A. Niemann extracted a pharmacologically active crystalline alkaloid from the dried leaves and appended the Latin chemical suffix, *-ine*, to the word, *coca*, thus producing the new word, *cocaine*.

About this time the Italian neurologist Paolo Mantegazza published his monograph on the hygienic and medicinal virtues of coca.² He self-administered coca leaves by chewing graded amounts while recording his subjective feelings, describing the delirium of coca intoxication as follows:

I felt extremely happy . . . I began to shut my eyes involuntarily and the most splendid and unexpected phantasmagoria started to flit before my eyes. I was at that time fully aware of myself, but I felt isolated from the external world and saw images that were more bizarre and splendid, in terms of color, than could ever be imagined. Neither the brush of the most brilliant painter nor the pen of the fastest stenographer could have transmitted for a single moment those marvelous apparitions, which were tied to each other not by relationships or associations, but through the whims of unleashed fantasy and a rich kaleidoscope. . . . Some of the images I tried to describe in the first part of my delirium were full of poetry. I sneered at the poor mortals condemned to live in this valley of tears while I, carried on the wings of two leaves of coca, went flying through the spaces of 77,438 worlds, each more splendid than the one before.

By 1886, preparations of coca leaves had entered the standard pharmacopoeia of the British Empire as an *infusum cocae* gargle for tonsillitis, as a *pastillus cocae extracti* for hay fever and spasmodic asthma, as *vinum cocae* for vomiting, as *emplastrum cocaineae* for neuralgia and sciatica, as *tabellae cocaineae* for sea-sickness and nausea of pregnancy, as *unguentum cocaineae* for eczema and shingles, as *vaselinum cocaineae* for burns and urethral catheters. This newly isolated alkaloid was generously dispensed to the Victorian public suffering from a variety of secular ills including ennui, depression, rheumatism, indigestion, toothache, as well as those seeking an appetite suppressant or an aphrodisiac. The crystalline substance was freely available in pharmacies and many notables including Robert Louis Stevenson, Charles Dickens, Thomas de Quincey, and Sigmund Freud proclaimed its mood-enhancing virtues.

Only a minority of medical practitioners expressed any misgivings over the darker side of cocaine, its capacity to induce addiction. One such physician, Arthur Conan Doyle, begins his famous 1888 story, *The Sign of the Four*, with the following description:

Sherlock Holmes took his bottle from the corner of the mantelpiece, and his hypodermic syringe from its neat morocco case. With his long, white, nervous fingers he adjusted the delicate needle, and rolled back his left shirt-cuff. For some time his eyes rested thoughtfully upon the sinewy forearm and wrist, all dotted and scarred with innumerable puncture-marks. Finally, he thrust the sharp point home, pressed down the tiny piston, and sank back into the velvet-lined arm-chair with a long sigh of satisfaction.

Three times a day for many months I had witnessed this performance, but custom had not reconciled my mind

to it. On the contrary, from day to day I had become more irritable at the sight, and my conscience swelled nightly within me at the thought that I had lacked the courage to protest. . . . I suddenly felt that I could hold out no longer.

"Which is it today," I asked, "morphine or cocaine?"

He raised his eyes languidly from the old black-letter volume he had opened. "It is cocaine," he said, "a seven-per-cent solution. Would you care to try it?"

The US Pure Food and Drug Act of 1906 declared cocaine to be a regulated substance requiring medical sanction for its use. By 1914, the Harrison Narcotic Act made the possession, sale or gift of cocaine a federal offense. Cocaine usage, now covert, persisted as a recreational drug in the United States, but was restricted largely to certain occupations and cultures, benevolently perceived and never becoming a major public health or police concern. In recent decades, however, cocaine has invaded the mainstream of illicit drug usage, assuming a major political and even economic role in the affairs of both South and North American nations. Its medical ramifications are now immense and we devote this issue of the *Journal*, under the guest editorship of Dr David Lewis, to a series of articles exploring the participation of coca in Andean cultures, its toxicology, its effects upon pregnancy, its role in adolescents and the dynamics of cocaine dependency.

Stanley M. Aronson, MD

References

- ¹ Plowman, T. The ethnobotany of Coca [Erythroxylon spp., Erythroxylaceae] Advances in Economic Botany, 1:62-111, 1984.
- ² Mantegazza, P. in, the Coca Leaf and Cocaine Papers, G. Andrews and D. Solomon, eds., pp. 38-42, Harcourt Brace Jovanovich, New York, 1975.

Physicians Have Been Drafted for the 'War on Drugs'

On September 15, 1986, President Ronald Reagan signed Executive Order 12564 establishing a Drug-Free Federal Workplace. Congress (Public Law 100-71; July 11, 1987) then mandated that each federal agency develop standards for all aspects of laboratory drug-testing necessary to carry out the Executive Order. By the end of 1987, about 24,000 federal employees in such sensitive areas as air-traffic control were screened for drug use and only then did the problem of false positives come to be appreciated. About 3% of a screened population will be declared as drug-positive, based on technically dictated limits of the radioimmune assay technic (RIA), the enzymes medical immunological technic (EMIT) and TDX methods for the following agents: marijuana metabolites; cocaine metabolites; opiates (morphine, codeine), phencyclidine and amphetamines (amphetamine and methamphetamines).

If, for example, 100 federal workers are screened, about three will be declared by the laboratory to be positive for one or more of the listed agents. Of these three, perhaps one or two will have a valid clinical reason to be taking one or another of these drugs. Once clinical justification is established, a physician may then change the laboratory designation of "positive" to "negative" by reason of legitimate medical usage. Thus, the "false positives" are between 33 and 66% of the total positives.

The government has now established the Medical Review Officer (MRO), a person whose function it is to review these positive drug results and if possible

convert them to negative results by means of history, physical and often further laboratory testing. According to the Federal Register, Volume 53, page 11,980, the MRO is said to be:

"A licensed physician responsible for receiving laboratory results, generated by an agency's drug testing program, who has knowledge of substance abuse disorders and has appropriate medical training to interpret and evaluate an individual's positive test results, together with his or her medical history and any other relevant biomedical information."

The MOR therefore stands between the laboratory which generated the results, and the employer. The MRO relieves the anxieties of both the laboratory and the employers who separately fear lawsuits for "wrongful discharge of the employee." It is also possible that some non-federal employers shall be using screening procedures as a pretext for discharging unwanted employees.

Few physicians in Rhode Island will provide medical advising to those federal agencies dealing with air-traffic, military personnel or civilians working in nuclear industries. Some may be responsible for the health of the Environmental Protection Agency workers; and some will be certifying truck drivers for the Department of Transportation or air traffic controllers for the Federal Aviation Agency.

Some Rhode Island physicians carry on a practice in occupational medicine and it is to this group that this editorial note is particularly directed. They may find themselves "drafted" into the role of the MRO. Should this occur, there is a National Institute of Drug Abuse (NIDA) telephone number to call (1-800-843-4971).

The NIDA office also offers advice and three texts for those who may need them:

- NIDA Medical Review Officer Manual
- Mandatory Guidelines for a Federal Workplace Drug Testing Program
- NIDA Research Monograph — 73: Urine Testing for Drugs of Abuse

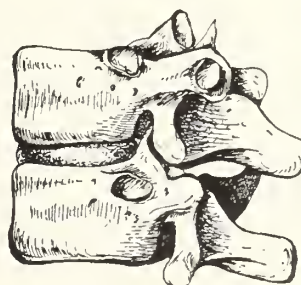
Elsewhere in this issue of the *Journal* is an article describing interpretive problems in urine testing for cocaine and its metabolites.

Horace Martin, MD, PhD
Department of Pathology
Rhode Island Hospital

The editors express their deep appreciation to the staff of the Brown University Center for Alcohol and Addiction Studies, and particularly Mr Stephen Oberbeck, for their invaluable assistance in conceiving and preparing this special Journal issue on the addictive properties of cocaine.

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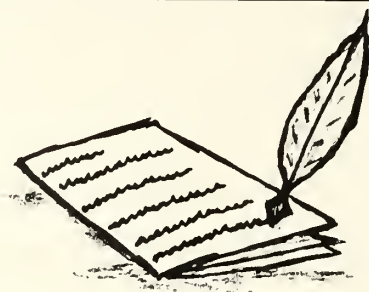
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EDITOR'S MAILBOX



The following are excerpts from "Letters to the Editor" in response to *The Medical Use of Fetal Tissue* (February 1990 RIMJ)

First, let me congratulate the editorial board of the RIMJ for bringing forth discussions of such a timely issue as fetal research. It is through this type of civilized discussion that we can educate our patients and the community at large on the complexities of abortion and fetal tissue research and the role of physicians as the "ethical interpreters and technical gatekeepers" of health.

In terms of having a child for the main purpose of helping a sibling survive through donation (such as the case in California a few weeks ago), I find it amazing that anybody would argue. Since the beginning of time, people have been brought into this world for the most trivial reasons. Who are we to say that having a child to help work the field, to satisfy a parental wish of a boy or a girl, to save a marriage or just to have an heir to the throne carries a higher moral justification than to save the life of a sibling?

Pablo Rodriquez, MD
Medical Director
Planned Parenthood of
Rhode Island

* * *

Unless a woman freely chooses to be pregnant the fetus has no "inalienable right" to remain in her body. In fact, forcing a woman to be pregnant against her will is one of the vilest forms of sexual abuse. Just as the act of sexual intercourse can be either an exalted expression of love or a brutal rape, so pregnancy can be either the most longed for event of a woman's life or a disaster of epic proportions. In the latter circumstance, abortion becomes a humane "cure" for a sexually transmitted "dis-ease." One and a half million women in the United States each year request and receive this cure from their physicians.

It is shameful that those who oppose the right to abortion have interdicted the potential additional cures that could result from the use of fetal tissue to pursue further knowledge and therapies.

Barbara H. Roberts, MD

PHYSICIANS IN THE NEWS

Recent appointments at The Memorial Hospital of Rhode Island include **Dr George Cooper, Jr, MD** to the staff of thoracic surgeons; **Dr Alicia D.H. Monroe** as residency director of the Family Medicine Residency Program; and **Dr Scott C. Early** to the department of family medicine.

* * *

Dr Joseph A. Latina was recently named Chief of the Division of General Surgery at St. Joseph Hospital. A member of St. Joseph's Medical Staff for 14 years, **Dr Latina** has a private practice in Cranston.

* * *

The Memorial Hospital of Rhode Island has been selected to participate in the International Study of Infarct Survival. **Dr Abdul Hakim Khan**, director of clinical cardiac pharmacology and continuing medical education at Memorial and associate professor of medicine at Brown University, is principal investigator of the clinical trials at Memorial. The study, which is being conducted in Europe and the United States, will compare the efficacy of three medications prescribed for dissolving blood clots occluding coronary arteries: streptokinase, tPA, and anistreplase.

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Dr. Holwick in operating room at Letterman Army Medical Center.

JANN L. HOLWICK, M.D.

General and Trauma Surgeon.
Captain, U.S. Army Reserve.

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“I spent six months looking into the Army Reserve program before I joined, wanting to make sure that my skill and time would be put to good use. I’ve been a Reservist three years now, and I still find it extremely rewarding. I have the satisfaction of knowing that I’m serving my country.”

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References

1. *USP DI Update*, September/October 1988, p 120.
2. *Br J Clin Pharmacol* 1985;20: 710-713
3. *Data on file*, Lilly Research Laboratories
4. *Scand J Gastroenterol* 1987;22(suppl 136): 61-70
5. *Am J Gastroenterol* 1989;84: 769-774

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Indications and Usage: 1. *Active duodenal ulcer*—for up to eight weeks of treatment. Most patients heal within four weeks.

2. *Maintenance therapy*—for healed duodenal ulcer patients at a reduced dosage of 150 mg h.s. The consequences of therapy with Axid for longer than one year are not known.

Contraindication: Known hypersensitivity to the drug. Use with caution in patients with hypersensitivity to other H₂-receptor antagonists.

Precautions: *General*—1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests—False-positive tests for urobilinogen with Multistix[®] may occur during therapy.

Drug Interactions—No interactions have been observed with theophylline, chlorazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in high-dose animals as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

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an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect, but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

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Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumentary—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

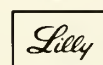
Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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Coca in the Andes: Traditions, Functions and Problems

Dwight B. Heath, PhD

There is no doubt that the unproblematic traditional uses of coca by pre-industrial Andean populations, and the positive functions such usage promotes, will diminish as the problematic uses of cocaine by industrial populations elsewhere increase.

Cocaine use in the United States has overshadowed the drug's ancient origins and cultural roots among its earlier, native users. This anthropological perspective will focus on what coca does for Indians who have traditionally used it in the Andes, and on how international drug traffic has affected them in recent years.

The source of cocaine is coca leaves,¹ which grow best in a distinctive, small ecological zone, in the tropics of South America. Less generally known is the fact that native populations in the high Andes of Bolivia, Colombia, Ecuador and Peru have been chewing

coca leaves customarily for centuries, with no ill effects.² How this cultural pattern evolved, and why it persists, are questions that highlight the complex interrelationships of biology and culture. Similarly, the impact of a burgeoning international trade in coca-paste and other derivatives has had important economic, political and other repercussions in those producing areas.

Traditions

Botanists believe the *Erythroxylon coca* bush probably originated in a few lush high valleys (called *yungas* in Bolivia or *ceja de la montana* elsewhere) cut into the eastern escarpment of the Andes. At an elevation of about 1,200-1,800 meters, such valleys are warm and moist throughout the year. Terracing holds moisture and increases the surface available for farming steep hill-sides.

A coca plant matures in about 3 years and continues to produce as many as 5 crops annually for 20 or more years. Clearly, a coca-grove has been

recognized for at least 500 years as a long-term investment by sedentary people oriented to a market system. This is still the case, even if the growers may appear both isolated (often living in dispersed homesteads and working miles from the nearest road) and traditional (maintaining not only their indigenous languages but also dress, religion, and many other practices from pre-Columbian times).

Despite its narrow area of cultivation, coca appears to have been traded throughout the vast chain of the Andes for millennia. Ancient remains of the leaf itself, distinctive wool shoulder-bags in which it was carried, and lime customarily ingested with it occur preserved in burial sites where human beings (and their stomach contents) are remarkably mummified and textiles retain their natural brilliant colors 800 years later. The coca tradition evolved in tandem with a sophisticated Inca civilization, which stretched nearly 3,000 miles from what is now Colombia well into Chile.

Dwight B. Heath, PhD, is Professor of Anthropology at Brown University. He has conducted extensive field research among several tribal and peasant populations, particularly in South America, has published extensively on the cultural role of alcohol and mood-altering drugs, and is a frequent consultant to governments and international organizations.

But why is there so broad a market for sun-dried coca leaves? And what does coca do for the people who habitually use it? For centuries, coca was a talisman in social, cultural and religious customs. One measure of its importance is the fact that, until a few years ago, poor Andean Indians rarely refused a handful of coca leaves to a beggar. This may be linked to the belief that one could not hope for a peaceful afterlife if one died without "the taste of coca." The leaves also played an important role in ceremonies associated with farming, births, weddings, burials, housebuilding and travelling. Coca was even invoked in a prayer-like refrain each time one took a few more leaves to "freshen the quid" ("Maria Santisima, Mamita kuquita, help me . . ."). As one leaves a stone on a cairn to mark a dangerous passage, other places — thought to be inhabited by spirits — are littered with balls of coca left by travelers.

. . . regardless of how virtuous one may have been in life, one could not hope to have a peaceful afterlife if one dies without "the taste of coca."

Further, as are tea-leaves or playing-cards in Western culture, the leaves can be "read" by a diviner to diagnose illness, predict the future, determine when best to plant, or where best to make a ritual sacrifice.³ Time is even measured by coca: "Oh, yes, we saw a plane pass overhead midway between the third and fourth coca-breaks." These ethnographic examples demonstrate the importance coca has long had for Andean Indians.

Until a few years ago, virtually all Andean Indian males above the age of 6 or 8 chewed coca most of their waking hours, and women

chewed it at least sometime daily in a ceremonial way. Actually, one does not "chew" but sucks a long-lasting quid tucked in the cheek, occasionally freshening it with a new leaf or two. Outsiders find their first chew painfully bitter. Regular coca users also periodically dab it with a preparation of lime — ground limestone or seashell often dipped on an elaborately carved spatula from a richly ornamented container. Spitting is frequent but not noisy; a few old-timers drool at the side of the mouth. The quid, about the size and shape of a big date or Brazil nut, bulges in the cheek but does not interfere with talking. Andean users do not relate to coca's playing any role in the Western addict's notion of "getting high" or "feeling a rush." Although investigators have described such motivations, they simply do not "ring a bell" among Andean users.

Functions

Then what are the rewards or reinforcements for coca-chewing? Historically, coca use has been the critical defining characteristic of Andean "humanity." As early as 1550, chroniclers of the Spanish conquest, both rustic conquistadors and educated friars, asked Incas and got answers both simple and sophisticated. "It's the custom," says much but reveals little. "I am an Indian, and to be Indian is to chew coca," provides manifold meaning for the anthropologist. Later native informants have provided more practical answers: "It relieves hunger." "It gives me strength." "I am less thirsty chewing coca." "With a little coca, we can overcome fatigue and work longer."

To be sure, cocaine is one of the principal alkaloids (among more than 15) in coca, clearly a central nervous system sympathomimetic. Central stimulation

does, in fact, mask sensations of fatigue. Vasoconstriction and increased muscular activity raise body temperature, and atropine triggers a rise in blood glucose levels. Nor have minimal levels of cocaine released by "chewing" ever been implicated in habituation or "psychological dependence," much less in tolerance, "physiological dependence" or "addiction." Jaffe's basic text on pharmacology⁴ made this point even before he moved to a behavioral definition of addiction that social scientists savor as an indication that our work is finally being recognized as valid and relevant in some biomedical sciences.⁵

In short, pharmacologists have finally found in laboratory studies that the reasons Indians gave for chewing coca make sense. Anthropologists considered gullible for trafficking in "anecdotal evidence" or "mushy journalistic impression" have been able to enjoy some vindication.

To afford some idea of the scale of operations, we are talking about a leaf no bigger than a bayleaf, picked by hand and dried in the sun, packed in bales, called *cestos*, weighing about 32 pounds and roughly a cubic yard in volume. It takes a huge quantity of leaves — and labor — to make up 5,000 tons of coca that was fully taxed and *legally* marketed in Bolivia in 1972, less than 1% of which was used to produce cocaine hydrochloride for sale abroad by the government, and only 3% of which was exported in leaf-form. There was virtually no illicit export at that time.⁶

To be sure, Indian "chewing" is not the only domestic use of coca. Newcomers to Cuzco or La Paz are often amazed to find that posh tourist-oriented hotels list coca-tea on their menus, and the infusion is highly recommended as a palliative for *sorroche*, the

"altitude sickness" causing nausea, headache, and cardiac arrhythmia in some people unaccustomed to only half as much oxygen as at sea-level.

A couple of Peruvian physicians gained some notoriety in the 1950s by offering a clear and simple physiological explanation for the custom of coca-chewing. Gutierrez-Noriega declared: "the main cause of the coca habit is the deficiency of foodstuffs in the affected areas — one begins to chew coca to suppress hunger but later the subject loses his appetite and eats little because he chews coca." His colleague Zapata-Ortiz followed suit: "... lack of food is the principal cause of cocaism."⁷

An alternative explanation of coca-chewing is in anthropologist Ralph Bolton's "hypoglycemia hypothesis." Bolton⁸ remarked on the high incidence of aggression among the people he calls "Qolla" (whom most other authors have called "Aymará").

There are many communities in which coca use is the defining characteristic of "humanity," and those who ignore it are beyond the pale.

Bolton also found glucose homeostasis problems widespread and asserts they are causally related to aggression. Assuming that the human organism attempts to maintain nominal glucose levels and that adrenal exhaustion or liver disease interfere with internal metabolic processes providing such homeostatic adjustment in a healthy system, then anger and aggression may serve as emotional and behavioral means of boosting glucose levels. Hypoglycemia also triggers hunger — a cue for Andean Indians to chew coca, which raises the glucose level (according to Bolton,

presumably by stimulating transformation of glycogen stores). Coca is not a primary factor in his analysis; he pays much more attention to vitamin-mineral deficiencies and protein, a high cirrhosis rate, land shortage, erratic food production and hypoxia as well. In a sense, "the hypoglycemia hypothesis" can be viewed as a special variant of "the food scarcity hypothesis," since both posit coca as a food substitute.

But man cannot live by coca alone; not even *Homo andinus* — a Peruvian physician less than 50 years ago wrote about Andean Indians as a distinct species.⁹

Note that Frombach has demonstrated, in scientifically convincing ways, that coca-chewing does, in fact, raise blood glucose levels quickly and for several hours.¹⁰ At about the same time, Montesinos and Nieschulz and Schmersahl were demonstrating that cocaine may be relatively unimportant among the many alkaloids released in traditional coca-chewing — the addition of alkaline does facilitate the extraction of alkaloids from the leaf, but only by degrading cocaine, leaving ecgonine the major product (among over a dozen) of hydrolysis and metabolism.¹¹

This may help explain the "fuzzy data" in ethnographic accounts of heavy eating by coca-chewers. Though virtually unanimously reported, they were previously thought to be of questionable validity. While it is true that Andean Indians are often under- or malnourished, this doesn't mean they decline to eat heartily and with great gusto when the opportunity arises. Coca apparently makes one's hunger easier to bear when no food is available, but certainly does not suppress, or even dull, one's eagerness to eat whatever may be available. In fact, coca-chewing and eating are often combined in a single event. Tan-

talizing hints from ongoing pharmacological studies at McGill University suggest that yet another alkaloid in coca interacts with certain carbohydrates to significantly enhance their nutritional value — but that this occurs only above a certain altitude.¹²

In the pharmacology of coca, as traditionally used in the Andes, cocaine seems relatively unimportant, and the habit is neither a vice nor a disease.

I won't burden you with the full details in this anthropologist's list of what's good about coca in sociocultural terms, but don't overlook close to 1000 mg of calcium a day from the lime (in an area where the native diet is low in calcium), and high levels of vitamins B₁, B₂, and C (also relatively lacking in Andean diet.) Serum protein levels of chewers do not differ significantly from those of nonchewers.

In short, coca is refreshing, medicinal, and healthful, as well as being often also symbolic and mystical for Andean Indians. But it is no substitute for food. Neither is it a "drop-out drug," sought for a feeling of "rush" or to achieve a "high." In the Andes, the cocaine habit is neither vice nor disease.

Problems

In spite of positive social, cultural, and biological functions that coca serves, it also has resulted in serious problems in recent years, even among Andean Indians. The problems do not result from traditional uses but from increasing diversion of coca to the illicit international market, "narcotrafficking" in "hard drugs."¹³ Little sense of guilt, nor even much awareness of coca-related problems elsewhere, afflicts An-

dean growers and traditional users. They care little about addiction, the crime or violence by dealers or users in faraway cities or the cost in money and civil liberties of North American's "drug-war."¹⁴

They *do* feel the impact of national policies to thwart cocaine use and control its market, which expanded with such rapidity during the past decade. That feeling becomes an immediate threat when the US Drug Enforcement Agency or armed forces physically destroy a coca-planting by cutting, burning, uprooting, or with herbicide. The potential for physical violence is high, but, apart from that, immediate economic loss is sustained and, with herbicides, serious ecological damage is incurred. Prospects for crop-substitution are dim, until farmers are offered an alternative that is worth as much as coca; those offered so far have yielded less than one-fourth as much profit.

Even successful growing and sales results in problems. The production of crude cocaine paste has made millionaires of ambitious entrepreneurs in the Andean countries.¹⁵ However much they may spend abroad, they also spend lavishly at home. Like latterday Robin Hoods, they have been known to pave the streets, provide lighting and water systems in towns that never had them, and to help poor and sick neighbors in ways that their governments never did. But the scale and motives of such largesse can be problematic and suspect — when the legal system becomes a tool of the drug-runners, lawlessness becomes the norm, or the armed forces devote more time, energy and money to participating in drug-traffic than to public works.

Jobs are created, and peasants are happy to earn more in a night

of "stamping coca" than they could in a month of agricultural labor — but life-expectancy in such a job is very low. Constant immersion up to the calf in kerosene and sulfuric acid doesn't necessarily kill them, but it often incapacitates them in a year or less. We don't really know what will become of those "disposable people," but the outlook is not good — especially when so many are also brain-damaged from having smoked *bazuco*, cocaine-paste in cigarettes, often an integral part of the pay for such work.

There is a special ironic twist to all of this. As people in faraway places use a highly refined derivative of the native coca leaf . . . many of those whose ancestors domesticated it and used it as both a sacred and secular adjunct to many of their workaday activities find that it has been priced out of their reach.

The fragile ecology of the Amazon Basin is being assaulted not only by large-scale deforestation for short-lived cattle-ranches, but also by the pollution from random dumping of waste-products (kerosene, diesel fuel, sulphuric acid, and ether are among the most common toxins) that result from the conversion of coca leaves to cocaine. As a rule-of-thumb, roughly a ton of leaves yields 5 kilograms of cocaine-paste, which in turn can be further refined to produce about 2 kilograms of cocaine-hydrochloride.

From an anthropological point of view — and from the point of view of the Indian population who cherish their traditions — there is a special ironic twist to all of this.

As people in far-away places use a highly refined derivative of the native coca leaf — sometimes with a titillating sense of danger — many of those whose ancestors domesticated it and used it as both a sacred and secular adjunct to many of their workaday activities find that it has been priced out of their reach. Beggars no longer can be assured of a handout of coca; fewer coca leaves are used in rituals; and not all peasants who would like to chew (in a way that can perhaps best be compared to a US coffee-break or a UK tea-time) can afford to do so in today's market.

What the consequences of such a shortage — at the very source of the world's supply — may mean in the long run, in terms of nutrition, aggression, and ancient customs, I leave to others to predict. But there is no doubt that the unproblematic traditional uses of coca by pre-industrial Andean populations, and the positive functions such usage promotes, will diminish as the problematic uses of cocaine by industrial populations elsewhere increase.

References

- ¹ The best general introduction to coca and cocaine in social and historical context is Lester Grinspoon and James B. Bakalar, *Cocaine: A Drug and Its Social Evolution* (rev. ed.), Basic Books, New York, 1985; an earlier effort at setting the subjects in a broadly interdisciplinary perspective is itself of historical interest: W. Golden Mortimer, *Peru: A History of Coca, The "Divine Plant" of the Incas*, J.H. Vail, New York, 1901.
- ² Ethnographic studies that provide detailed information on traditional beliefs and practices among Andean Indians are numerous. Among the most interesting, insightful, and accessible are Catherine J. Allen, *The Hold Life Has: Coca and Cultural Identity in an Andean Community*, Smithsonian Institution Press, Washington, 1988, and Joseph W. Bastien, *Mountain of the Condor: Metaphor and Ritual in an Andean Ayllu*, Wave-land Press, Prospect Heights, IL, 1985. Although many anthropologists have considerable familiarity with the production and marketing of coca and cocaine, it is difficult to imagine how to write something that would be substantively meaningful with respect to the most recent devel-

opments without incriminating our friends and informants.

³ Some of these traditional usages are vividly portrayed in excellent documentary films *The Spirit Possession of Alejandro Mamani, Magic and Catholicism*, and *Potato Planters* (American Universities Field Staff), Hanover, NH, 1974.

⁴ Jaffe JH, *Textbook on Pharmacology*, Jossy-Bass, St. Louis, 1975.

⁵ Jaffe pioneered among biomedical scientists in insisting that addiction could best be conceived in terms of what people would do to get certain effects, rather than in terms of physical dependency: "Drug Addiction and Drug Abuse," pp. 535-584, in Gilman AG, Goodman LS and Gilman A, eds., *The Pharmacological Basis of Therapeutics* (6th ed.), Macmillan, New York, 190.

⁶ The explosive growth of coca cultivation for the illegal international drug trade is dramatically illustrated by the estimate that, by the mid-1980s, 20 to 30 thousand tons were being converted into cocaine paste for shipment to Europe and Asia annually, and about 70 thousand tons to the United States ("The Supply of Illicit Drugs to the United States from Foreign and Domestic Sources in 1985 and 1986," *National Narcotics Intelligence Consumer's Committee*, Washington, 1987).

⁷ The "food scarcity hypothesis" about Indian coca-chewing is best represented in the works of Carlos Gutiérrez-Noriega and Vicente Zapata-Ortiz (various dates, but collected in their joint *Estudios sobre la coca*

y la cocaína en el Perú, no publisher, Lima, 1947).

⁸ Bolton R, "Aggression and Hypoglycemia among the Qolla: A Study in Psychobiological Anthropology," *Ethnology* 12:227-257, 1973.

⁹ Heath DB, "Peasant Syndicates among the Aymara of the Yungas: A View from the Grass-Roots," in Landsberger, H (ed.), *Latin American Peasant Movements*, Cornell University Press, Ithaca, NY, 1969.

¹⁰ Monge C, *Acclimatization in the Andes: Historical Confirmation of "Climatic Aggression" in the Development of Andean Man*, Johns Hopkins University Press, Baltimore, 1948.

¹¹ Montesinos, F, "Cocaine metabolism," *Bulletin on Narcotics* 17:11-19, 1965; and Nieschulz O, and Schmersahl P, "Untersuchungen über die bedeutung des kalkzusatzes beim kauen von coca-blättern," *Pharmakologische und Phytochemiste Abteilung* 10:178-183, 1969.

¹² Personal communication, November 1989.

¹³ Much of what is written about the international drug traffic is either sensationalistic and grossly inaccurate, or polemical and devoid of substance. Exceptions are *Drugs in Latin America* (Publication 37, Studies in Third World Societies, Williamsburg, VA, 1987), and Edmundo Morales, *Cocaine: White Gold Rush in Peru*, University of Arizona Press, Tucson, 1989. See also note 8, above.

¹⁴ Reasons for the chronic failure of US "wars

on drugs" are clearly and succinctly spelled out by Edward M. Brecher, "Drug Laws and Drug Law Enforcement: A Review and Evaluation Based on 111 Years of Experience," *Drugs and Society* 1(1):1-27, 1987.

¹⁵ The meteoric rise of what US officials call "drug-lords" in Bolivia is described in rich detail by Lesley Gill, in her *Peasants, Entrepreneurs, and Social Change: Frontier Development in Lowland Bolivia*, Westview Press, Boulder, CO, 1987.

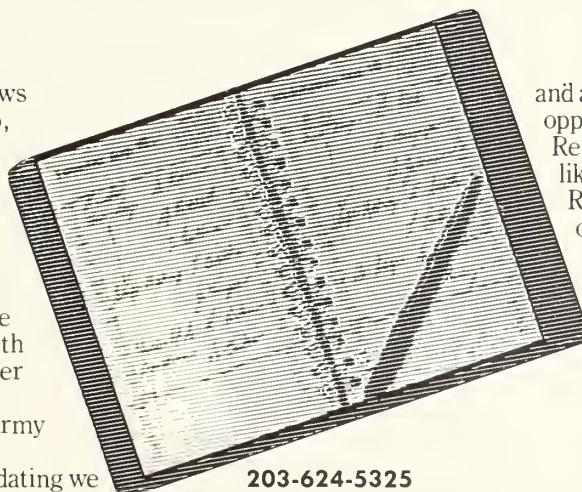
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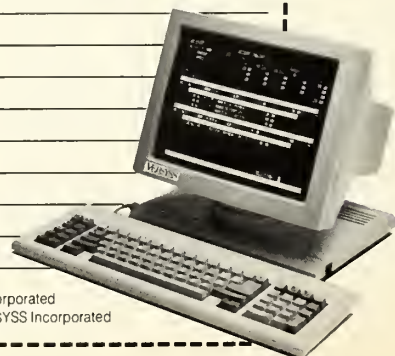
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Cocaine in Body Fluids: Analysis and Interpretation of the Drug Abuse Specimen

Horace F. Martin, PhD, MD

The advent of thin-layer chromatography and gas chromatography . . . made routine analysis possible, but still time consuming and labor intensive.

America is experiencing its second epidemic of cocaine addiction in this century. The first occurred at the turn of the century. In 1906, more cocaine per capita was consumed than the usage today. This first epidemic was successfully controlled by concerted governmental activity spearheaded by the Harrison Narcotic Act. Cocaine addiction was nearly eradicated in America for 40 years.

For a variety of social and moral reasons, cocaine addiction started for the second time in recent years.

New analytic methods for the detection of cocaine are now sensitive enough to detect the drug in body fluids. Laboratory performance of these new methods are evaluated by a new federal agency, the National Institute of Drug Abuse (NIDA), for purposes of accrediting drug-testing facilities. The focus for control has a new dimension, the identification

of the abuser by means of drug testing. Because the Supreme Court has already said that government employees must submit to a urine test if they wish to continue to be employed, many more Americans may experience intrusion by government into their personal lives.

Cocaine: Isolation and Structure

An Austrian explorer, Dr Scherzer, brought coca leaves to Vienna from South America in 1859. Samples were sent to Friedrich Wohler, professor of chemistry at Gottingen. He, in turn, assigned the isolation of the alkaloid to Albert Niemann, his graduate student. In 1860, Niemann extracted the leaves with 85% alcohol that had been acidified with 2% sulfuric acid. The extract was treated with calcium carbonate, filtered and then neutralized with sulfuric acid. The alcohol was removed by distillation. The syrupy residue was treated with water to separate resin, and then precipitated with sodium carbonate. The solid residue was extracted with ether and the ether removed by evaporation. The cocaine obtained was in the form of colorless crystals. This method of extraction re-

sulted in a low yield of product due to hydrolysis of the esters in cocaine. As can be seen in the optimized structure (Figure 1) cocaine consists of a seven-membered alopahatic ring with a three-membered N-methyl bridge, with methanol and benzoyl esters. After hydrolysis, cocaine yields methanol, benzoic acid and ecgonine. Carl Liebermann, professor of chemistry at Berlin, prepared cocaine by first hydrolyzing the cocaine to ecgonine (Figure 2). This was followed by re-synthesis of the methyl ester by bubbling dry hydrochloric acid into ecgonine dissolved in methanol. This ester when treated with ben-

ABBREVIATIONS USED:

DHHS: Department of Health and Human Services

EMIT: enzyme multiplied immunoassay technic

FPIA: fluorescence polarization immunoassay

GC: gas chromatography

GC/MS: gas chromatography/mass spectrometry

HPLC: high pressure liquid chromatography

NIDA: National Institute of Drug Abuse

RIA: radioimmunoassay

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zoyl chloride yielded cocaine from the ecgonine methyl ester (Figure 2). The yield, by the re-synthesis procedure was about 1 gram of cocaine from 50 grams of coca leaves.

Cocaine: Select Pharmacology

When 100 mg of cocaine is administered intravenously, by chewing, by intranasal application or inhaled (as free base) in a 70 kg subject, the cocaine hydrolyzed nonenzymatically to benzoylecgonine. The benzoylecgonine is non-specifically hydrolyzed to ecgonine and benzoic acid by pseudocholinesterase in the red blood cell. These are the major metabolites found in the urine. There is a minor pathway that involves demethylation of the methyl group in the N-methyl bridge. Consequently, there are three demethylated minor metabolites corresponding to the ecgonine, methyl ecgonine ester and benzoylecgonine parent compound. The half-life of cocaine in blood is about one hour and the volume of distribution is about 1.5 liters/kg. The amounts found in urine at the end of 24 hours are shown in Table 1. The earlier analytical methods for investigating these substances in the urine were dependent on physical methods based on microscopy, ultraviolet and infra-red spectroscopy. Column and paper chromatography were the choice methods for separation.

Chewing 5g of *Erythroxylon coca* leaf will cause 20-50 mg of cocaine to be ingested, producing a peak plasma concentration of about 0.1 mg/ml in about one hour.

Although these methods were perfectly adequate for studies of urinary excretion and cumulative

toxicity at the 5 mg/ml range, they were insensitive for pharmacokinetic studies. In 1951, Woods, Cochin, and others developed a method based on the observation that minute amounts of organic amines added to bromophenol blue in benzene or chlorobenzene produced an intense yellow color and the optical density was a linear function of the concentration of the amine. The general method was to extract the amine from the fluid with a halogenated hydrocarbon, filter the extract, or by use of a sucrose column to remove the excess water and other interfering materials mixing the filtrate with bromocresol blue in the same solvent yielded a detectable color. Re-extraction was used to concentrate and remove interfering substances. This method enabled detection of concentrations as low as 0.5 mg/ml. This method, while sufficiently sensitive and specific, was, however, time-consuming and impractical for mass screening. The advent of thin-layer chromatography and gas chromatography utilizing a nitrogen-sensitive detector made routine analysis possible, but still time-consuming and labor intensive. Nevertheless, these methods made it possible to define blood concen-

tration, metabolism, excretion and toxicity of cocaine in relation to diverse routes of administration.

Blood Levels

Chewing 5 g of *Erythroxylon coca* leaf will cause 20-50 mg of cocaine to be ingested, producing a peak plasma concentration of about 0.1 mg/ml in about one hour. If the average 70-kilo person inspires intranasally ("snorts") 140 mg of cocaine, the plasma concentration is 0.1-0.15 mg/ml at the end of one hour. The oral route results in a higher plasma concentration by a factor of 2 when compared to the maximum levels achieved by the intranasal route. Either route takes about one hour to achieve peak effect and elimination occurs at a rate defined by a one hour half-life. A 32 mg bolus results in a plasma concentration of 0.3 mg/ml in 5 minutes. Nasal topical application of 100 mg achieved plasma concentrations of 0.3 mg/ml in one hour. In this study, the rate of elimination was slower than that reported previously, and these authors reported a half-life of about 4 hours. It has been reported that elimination kinetics are dose-dependent in the range of 50-200 mg per single dose. Co-

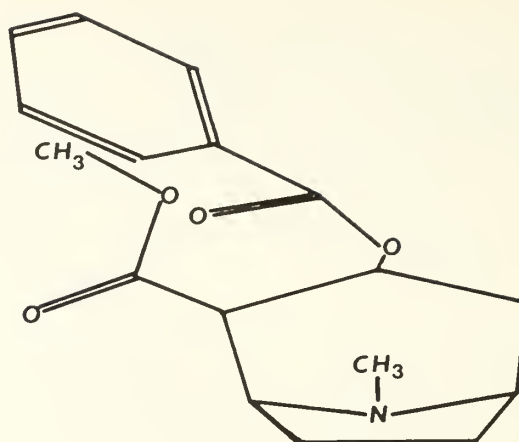


Figure 1. Cocaine (Free Gas State)

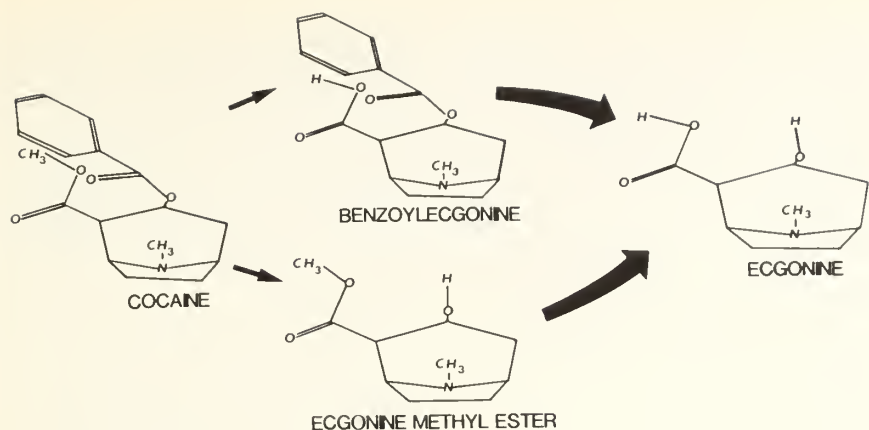


Figure 2. Hydrolysis

caine has also been administered vaginally and caused death in one case reported this year. Other routes of administration are intramuscular, sublingual, and rectal.

Chronic abusers, who smoked cigarettes containing 75 mg of cocaine, developed plasma concentrations of 0.25 to 0.9 mg/ml. Herbal tea is yet another mode of ingestion; but, there is as yet no pharmacokinetic data on this route. "Free-base," the purified street nonhydrochloride, ie, the amine free base, when "snorted" has a rapid onset of action occurring in 5-10 minutes and a duration of action of about one hour.

Toxicity

Cocaine is brought into the United States illegally from South America, where it is extracted and refined to form the hydrochloride salt. The cocaine is "cut" with mannitol, lactose, glucose, or cornstarch. The most common route of abuse is intranasal or "snorting."

Overdosage with cocaine is relatively rare. Cocaine toxicity is due to the drug's ability to block catecholamine uptake at adrenergic nerve endings. The lethal toxicological sequence due to cocaine overdose often is: intense paranoia, bizarre and violent behavior, hyperthermia, and sudden collapse due to myocar-

dial infarction, ventricular tachycardia, fibrillation, or alternately, cerebrovascular accident. Treatment is possible. For example, one patient swallowed 5 gm in a packet; the convulsions that resulted responded to therapeutic intervention, and he survived. Plasma levels were reported to have reached 5.2 mg/ml. While the fatal dose in man has been estimated at 1.2 gm fatal arrhythmia may arise following much smaller doses. The use of nitrendipine, a calcium channel blocker, has been recommended for control of arrhythmias in cocaine overdose. Correction of acidosis helps in stabilizing rhythm. Medical Examiner autopsy studies have noted evidence of cocaine-induced cardiotoxicity. Compared to a similar size cohort who succumbed to trauma, the cocaine-exposed group had far more myocarditis (mononuclear infiltrates). This was felt to be related to microvascular injury. The prevalence of contraction band necrosis, which had previously been reported to be highly associated with cocaine myocardial toxicity, was found to be mainly associated with sudden traumatic death, rather than a direct effect of cocaine on the heart. In fatalities, the blood concentrations have been reported to be in the range of 0.5-20 mg/ml per kg of

brain, liver, and kidney. Urine levels were 0.1-215 mg/ml.

Mandatory Drug Screening

Today, 33 government agencies are enlisted in the war on drugs. NIDA, the leading agency for drug abuse research, has a mission to "sponsor and conduct research into incidence and prevalence of drug abuse, its causes, consequences and approaches to prevention and treatment."

NIDA, one of three research institutes in the Alcohol, Drug Abuse and Mental Health Administration, is buried deep within the Department of Health and Human Services (DHHS). "It's a fourth-level bureaucracy with absolutely no clout," says Robert Dupont, a former director of NIDA. The *White House Conference on a Drug Free America* reported to the President that: "NIDA has grown into an overly bureaucratic agency that has lost sight of its mission."

The Current Analytical Methods

The analytical sciences have provided us with the tools to measure drugs in urine in the workplace. The new tools can be classified into one-step immunoassay methods, and two-step assays. The one-step assay methods are: radioimmunoassay (RIA), enzyme multiplied immunoassay technic (EMIT), and fluorescence polarization immunoassay (FPIA). Two-step assays are those that have two operations in sequence. The first is separation, accomplished by gas chromatography (GC) or high pressure liquid chromatography (HPLC). Detection is often accomplished within the same instrument that does the separation; however, these operations can be done in separate instruments. Compounds separated by gas chromatography can be detected either by a nitrogen-selective detector, electron capture or by mass spectrometry.

The one-step methods are based on immunological principles. All three methods: RIA, EMIT, and FPIA, have as their foundation an antibody that interacts reversibly with the drug. In the case of radioimmunoassay, detection is a function of radioactive particle ionizations counted by a detector. In EMIT methods, the drug's attachment to the protein antibody causes an enzyme to become activated and react with substrate. The amount of drug is proportional to either product or cofactor, production or consumption. The wonderful advantage of this method is that by investing time, there is increased analytical sensitivity of drug detection. FPIA is dependent on the angle of the plane of the emitted light at a specific wave length. A small, free-tumbling molecule fluoresces (emits quanta) in all possible planes. As a result, light is not *polarized* in any particular plane. But, if the molecule is large, movements are slow and lumbering. After excitation, the molecule has 0.1 of a billionth of a second to return to some lower state by fluorescence. In that infinitesimally small time, the large lumbering molecule can't change its position and consequently all of those fluorescent molecules emit their quanta 90 degrees to the angle of their excitation. When it is said that the molecule is polarized, many quanta are aligned at the same angle (plane).

A drug, conjugated to a fluorescent dye and subsequently attached to a large protein, results after excitation in polarized fluorescence, this being proportional to drug concentration. What is done in practice is to label an antibody with a fluorescent dye. In fact, two labelled antibodies are used, one with the fluorescent indicator attached and the other with a quencher of fluorescence.

Both antibodies, one containing the fluor and the other labelled by the quencher, have sites for attachment to the drug. Consequently, when a drug is present, the fluor and the quencher are brought together thus quenching the polarized light. In this variant of the FPIA assays, the amount of polarized fluorescent light is inversely proportional to the amount of drug.

Current Practice

For 35 to 45 dollars per specimen, private employers can now contract with commercial laboratories, to analyze and supply a container, with labels ready to document the chain of custody. Commercial laboratories supply a sealable plastic envelope which is closed by attaching labels that have been signed by the sender and the receiver. These are then forwarded to selected commercial laboratories, namely, those laboratories that have invested \$17,300 for NIDA certification. Today, more than 50 such laboratories exist.

These laboratories will screen the specimen by the rapid immunological one-step method for a limited set of agents: marijuana, cocaine, amphetamines and opiates. Interestingly, most employers do not test for alcohol either in preemployment or random testing.

If an individual challenges the reported results, different laboratories have different policies. For example, the large military laboratories make available the specimen for retesting by an independent laboratory. Commercial laboratories, on the other hand, will retest the sample themselves, but may not make the specimen available for retesting at an independent laboratory.

If the test is positive for cocaine at levels higher than the chemical sensitivity of the assay (typically

0.3 mg/ml), that specimen will be further analyzed by gas-chromatography/mass spectrometry (GC/MS) for definitive identification. A definitive test is necessary because the immunological one-step tests are subject to cross-reactivity of other structurally similar molecules (eg, drinking herbal teas result in false positive results by some screening tests). Mass spectrometry is definitive because it fragments the molecule into small molecular units that have a unique pattern, with very high probability of correct chemical identity.

Overdosage with cocaine is relatively rare. Cocaine toxicity is due to the drug's ability to block catecholamine uptake at adrenergic nerve endings.

Many physicians in the Rhode Island community maintain a minor practice in occupational medicine. Such physicians may be approached by an employer to formally interpret drug screening results, to refer employees for counseling and detoxification, and perhaps, to participate in their rehabilitation.

Epidemiologic Considerations

Given that the prevalence of cocaine abuse in a screened population is 3%, and that the epidemiological sensitivity and specificity are both 95%, it has been estimated that the chance that a true positive exists among the entire population of positive tests is only 35%. This means, after retesting there is only one chance in three that this positive result for cocaine will remain positive. The major reason for this low significance of a positive result is due to the low prevalence. A secondary reason is that there are interfering substances that will

Table 1 The Major Metabolites of Cocaine in Urine at end of 24 Hours

Metabolite	Time (Hours)		
	Excreted	Maximum	Disappears
Cocaine	1-9	1	12
Benzoyllecgonine	35-54	4-8	48-72
Ecgonine methyl ester	32-49	0-8	24-48

effect the analysis. Urine is a very complex media and the ordinary constituents of urine greatly affect the screening result of the immunological methods. Some substances in concentrations greater than 100 mg/ml will cross-react with the screening immunoassay. These assays have a chemical sensitivity of 0.3 mg/ml. The typical FPIA assay has a cross-reactivity of 2% between the cocaine and the ecgonine methyl ester. Another factor that clouds the interpretation is variable rates of elimination.

NIDA . . . has a mission to "sponsor and conduct research into incidence and prevalence of drug abuse, its causes, consequences and approaches to prevention and treatment."

The duration of detection is two days for cocaine and up to three days for the cocaine metabolites. A clinical axiom has evolved that the presence of benzoyllecgonine in the urine proves that cocaine use has occurred within the past two-three days. This axiom like other generalities is limited. The rule was developed from experimental, one-time, low-dose exposures, but in the addicted individual, who has been using gram amounts of cocaine per day, benzoyllecgonine can be detected for 10 to 20 days after cessation of cocaine abuse. Diseases, related or unrelated to drug abuse, may modify rates of cocaine metabolism. Multiple drug addic-

tions (eg, valium and cocaine) will also modify elimination half-life. Therefore, finding a positive result in a chronically addicted individual 5 or 10 days after the first result is the rule and not the exception.

Correct interpretation becomes exceedingly difficult. When the United States Navy began its drug testing program in 1981, the Oakland laboratory was swamped and quality control was neglected, with the result that the Navy had to reverse all positive findings for the period that it failed to document quality control. Today, that facility invests 20% of its cost of operation on quality control and has contracted with an independent group to inspect that laboratory every two months. The Federal Aviation Administration had trouble with the toxicology laboratory at the Civil Aeromedical Institute in Oklahoma City, and the laboratory was disbanded for incompetence.

In the end, a physician must provide the final diagnosis. It will be a clinical synthesis of all the facts in the history, the social setting and the laboratory data.

In the end, a physician must provide the final diagnosis. It will be a clinical synthesis of all the facts in the history, the social setting and the laboratory data. The diagnosis of impaired function secondary to cocaine abuse will be based on the correlation of the extent of impairment with the drug

level (if available) and the pattern of drug abuse. Impairment is the key and that is what the physician will have to attest to, in order to prevent harm to the employee, himself, his coworkers, or other members of society.

State agencies need the physician's certification of addiction/impairment to authorize health care payments for treatment and rehabilitation.

In summary, the presence of a drug in the urine is simply proof of past ingestion. The issue is impairment in the workplace, which chemical tests alone cannot measure.

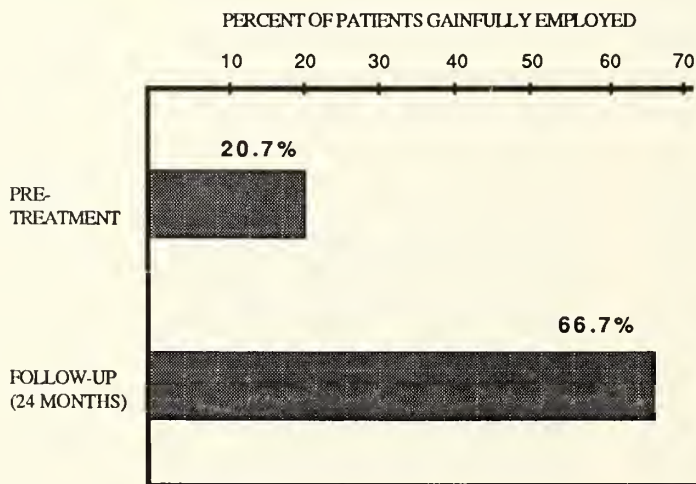
References

- Allen D. The cocaine crisis. Plenum Press, New York; p 10, 1987.
- ibid*, p 10.
- ibid*, p 10.
- National Treasury Employees Union v. Von Raab; 109 US 1384 (1989) and Skinner v. Railway Labor Executives' Assn; 109 US 1402 (1989).
- Strichartz G. Opus cit, p 3.
- Remington J, Wood H. The dispensary of the United States of America, 20th ed, JB Lippincott, Philadelphia, p 359-369.
- The structure was optimized for the free gas state using N Allinger Force Field Optimization 1985 update, Quantum Chemistry Program Exchange, Program No MMP2 (85). Indiana University, Bloomington, Indiana.
- Remington J. Opus cit, p 360.
- Baselt R. Disposition of toxic drugs and chemicals in man, 3rd ed, Year Book Medical Publishers, Littleton, MA; p 209, 1989.
- ibid*, p 209.
- Moffat A. Clarke's isolation and identification of drugs. The Pharmaceutical Press, London; p 489, 1986.
- Woods L, Cochran J. The estimation of amines in biological materials with critical data for cocaine and mescaline. J Pharmacol Exp Ther (101);189-199, 1951.
- Baselt R. Opus cit, p 208.
- Wilkinson P, Jatlow P, et al. Intranasal and oral cocaine kinetics Clin Pharmacol Ther (27);306-394, 1980.
- Greenland V, Delke I, et al. Vaginally administered cocaine overdose in a pregnant woman. Obstet and Gynecol (74);476-477, 1989.
- Baselt R. Opus cit, p 209.
- Hodgson E, Levi P. Opus cit, p 220.
- Baselt R. Opus cit, p 210.
- Goodman L, Gilman A. The pharmacological basis of therapeutics, 8th ed. The Macmillan Co, New York; p 376, 1965.
- Baselt R. Opus cit, p 210.
- Baselt R. Opus cit, p 210.
- Virmani R, Robinowitz M, et al. Cardiovascular effects of cocaine: an autopsy of forty

- patients. *Am Heart J* (115); 1068-1076, 1988.
- ²³ Baselt R. *Opus cit*, p 211.
- ²⁴ Booth W. War breaks out over drug research agency. *Science* (241);648-650, 1988.
- ²⁵ *ibid*, p 648.
- ²⁶ LeGrys V. American Association for Clinical Chemistry In-Service Training and Continuing Education (10);7-12, 1989.
- ²⁷ Baselt R. *Opus cit*, p 211.
- ²⁸ Moffat A. *Opus cit*, p 148 et seg.
- ²⁹ Rothstein M. Drug screening in occupational medicine March 14, 1908 University of Cincinnati. An outline is available of this valuable lecture on the limits of drug analysis (interfering substances).
- ³⁰ Siegel R. Cocaine in herbal tea(letter). *JAMA* (255);40, 1986.
- ³¹ Wells V, Halperin W, et al. The estimated predictive value of screening for illicit drugs in the workplace. *Amer J Public Health* (78);817-891, 1988.
- ³² In the Abbott TDx assay, there is less than 10% error in detecting benzoylecgonine in urine when there is protein at 50 mgs/deciliter; urea at 6 grams/deciliter. Bleach, peroxides and detergents will all significantly effect the urinary assay. Source: Abbott Laboratories, TDx Cocaine Metabolites p 22.52 or 829M, 1988.
- ³³ Abbott Laboratories, TDx Cocaine Metabolite, p 22.51 of 8298M, 1988.
- ³⁴ Poklis A. Evaluation of the TDx cocaine metabolite assay. *J Anal Toxicol* (11); 228-230, 1987.
- ³⁵ Weiss R, Gawin F. Case reports: protracted elimination of cocaine metabolites in long-term, high dose cocaine abusers. *Amer J Med* (85);879-880, 1988.
- ³⁶ Marshall E. Testing urine for drugs. *Science* (241);150-152, 1988.
- ³⁷ Marshall E. Testing urine for drugs. *Science* (241);150-152, 1988.
- ³⁸ *ibid*, p 152.

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Cocaine Use During Pregnancy

Donald R. Coustan, MD
Stephen R. Carr, MD

A recent, statewide, anonymous survey . . . revealed . . . that one of every 40 neonates born in Rhode Island has been exposed to cocaine 1-3 days before labor.

The epidemic of substance abuse has particular poignancy when the abusers are pregnant women who indirectly harm their developing fetuses. A recent statewide anonymous survey of all laboring women admitted to hospitals (Hollinshead, WH, et al: Statewide Prevalence of Illicit Drug Use by Pregnant Women — Rhode Island. MMWR 39:225-227, 1990) revealed the presence of cocaine or its metabolites in the urine of 2.5%, meaning that 1 of every 40 neonates born in Rhode Island has been exposed to cocaine 1-3 days before labor. This article outlines effects of cocaine on mother and fetus, and suggests

ways to manage such problems.

Pharmacology

Details of the pharmacology of cocaine have been covered elsewhere in this, and a previous issue, of the *Rhode Island Medical Journal*. However, to understand how cocaine affects pregnancy, we must review the mechanism by which this substance, previously considered to be innocuous, damages the fetoplacental unit. Increased concentrations of the neurotransmitters norepinephrine and dopamine at receptor sites may result in vasoconstriction, hypertension, myocardial irritability, and in some cases, seizures. Studies on pregnant ewes^{1,2} have demonstrated maternal vasoconstriction, decreased uterine blood flow, maternal and fetal hypertension, and fetal hypoxemia due to impaired oxygen transfer. Cocaine, of low molecular weight and high lipid and water solubility, is easily transported across the placenta and may, in fact, accumulate in the fetus.

Crack cocaine — an inexpensive easily portable, highly potent substance — is now widely used. Crack ingestion, usually by smoking, quickly raises blood cocaine levels because of rich pulmonary

circulation; the “high” is sudden and severe, as are the potential side effects. The effect is short-lived, leading to a desire to ingest more and more to maintain the high. Thus, effects on the fetus tend to be more severe with crack than with other forms of cocaine.

Effects on the Mother

The same complications which may occur in nonpregnant cocaine users can be expected to happen in pregnant women. Thus, acute myocardial infarction, cardiac arrhythmia, subarachnoid hemorrhage, stroke, rupture of the aorta, bowel ischemia all are possible.³ In fact, two cases of cocaine-associated maternal intracerebral hemorrhage during pregnancy and the postpartum period have recently been reported.^{4,5}

Effects on the Pregnancy

Interest in cocaine's effect on pregnancy first surfaced in 1983 when Acker and coauthors⁶ reported two cases of abruptio placentae occurring within a few hours after pregnant mothers took cocaine, one by needle and the other by “snorting.” Additional case reports over the next few years suggested that an association might be real. Among the nine

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series published to date, in which an association between cocaine use and abruptio placentae has been sought, six⁷⁻¹² have confirmed this complication. In the three¹³⁻¹⁵ which failed to confirm the association, the trend failed to reach statistical significance.

Therefore, it is extremely likely

Cocaine, of low molecular weight and high lipid and water solubility, is easily transported across the placenta and may, in fact, accumulate in the fetus.

that cocaine use during pregnancy can cause abruptio placentae, a life-threatening complication for both mother and fetus. The mechanism postulated for this association is decreased placental perfusion related to cocaine-induced vasoconstriction. Cocaine-induced hypertension may also play a role. One recent study¹¹ has suggested that abruptio placentae is more likely even among women who used cocaine only during the first trimester of pregnancy, raising the possibility that placental damage having occurred with early cocaine exposure may predispose toward abruptio later on.

Preterm labor and preterm delivery occur with increased frequency among cocaine-using mothers,^{7, 9, 12-15} a problem which may again be ascribed to decreased uterine blood flow. In 40 consecutive admissions for preterm labor to Women and Infants Hospital of Rhode Island recently reviewed (M. Pandiscio, unpublished data), cocaine or its metabolites were present in the urine of 13/40 (32%) mothers. Two studies have failed to demonstrate an association between cocaine use and cesarean section,^{10, 13} and an association with pregnancy-induced hypertension

seems possible¹⁶ but not definite.¹⁰ Finally, of four series in which an association was sought, three showed increases in spontaneous abortion rates among cocaine users.^{7, 8, 10, 17}

In sum, cocaine use in pregnancy appears to be associated with increases in abruptio placentae, preterm labor and delivery, spontaneous abortion, and possibly pregnancy-induced hypertension.

Effects on the Fetus and Neonate

Vasoconstriction with resultant decreased perfusion of the uterus might be expected to restrict nutrients to the fetus. Indeed, intrauterine growth retardation has been demonstrated in offspring of cocaine-using pregnant women in almost every study where it was sought.^{8, 10-13, 15, 18-19}

Anecdotally, neonatal nurses report that these babies are "difficult to comfort," and tend not to interact with their environment and caregivers.

Since cocaine readily crosses the placenta, direct fetal effects might be expected. At least one investigator has documented a case of cerebral infarction occurring *in utero*.²⁰ It might be anticipated that vascular compromise secondary to cocaine exposure during early gestation, the time of organogenesis, would cause birth defects. To date, six studies have sought such an association,^{8, 10, 13, 16, 21-22} and three^{8, 16, 21} have supported the possibility. However, to establish a causal relationship between the ingestion of any substance and congenital anomalies is very difficult; confounding variables (such as polydrug abuse or lifestyle differences) make interpretation problematic. Therefore, a link between cocaine and birth

defects must be considered tenuous at best at present.

Investigations of long term effects of *in utero* cocaine exposure on childhood behavior and mental/motor performance are just beginning to be reported. Anecdotally, neonatal nurses report that these babies are "difficult to comfort," and tend not to interact with their environment and caregivers. Signs of possible withdrawal have been reported in cocaine-exposed neonates.^{11, 18, 23} Two studies have reported that cocaine-exposed neonates are irritable, tremulous, and show poor organizational responses to their environment^{8, 24} and others have reported long lasting abnormalities of the electroencephalogram²³ and visual evoked potential. Some abnormalities in cocaine-exposed infants have been demonstrated through the first four months of life.²⁶ It is tempting to speculate that these problems in organization and interaction with the environment may tend to harm parent-infant bondings making child abuse and neglect more likely among these youngsters. This is particularly worrisome when one considers the hectic lifestyle of the cocaine-abusing parent, whose energies are consumed by the ever increasing need to procure drugs, leaving little time or attention for childrearing responsibilities.

Other Considerations

Most cocaine users do not limit themselves to use of one substance. Tobacco and alcohol must be considered "gateway substances" for cocaine and other drugs of abuse, and cocaine users often use not only these together, but also others such as marijuana, opiates, tranquilizers, amphetamines and barbiturates. Thus, adverse effects on the fetus may be compounded by maternal lifestyles or polysubstance use.

Nor are the mothers who abuse drugs the only problem. It is common for male sexual partners to be using, and often peddling, drugs, increasing the pressure on pregnant women to participate. Thus drug abuse in pregnancy must be viewed as a family disorder, and not an isolated individual problem.

Treatment

Options for treatment of cocaine abuse during pregnancy are currently limited. There is no chemical treatment for cocaine users similar to methadone for heroin addicts, which would satisfy the cocaine addict's compulsion to seek and ingest more cocaine. Since the environment of the cocaine user is an important part of the problem, most successful treatment approaches remove the individual from the destructive environment — either by inpatient detoxification or by group-living arrangements. Such approaches are expensive and usually crowded. Current federal, state and local initiatives can best deal with the drug abuse by increasing treatment opportunities, particularly for pregnant women and mothers of infants.

We believe a punitive approach to addiction, imposing criminal penalties for use during pregnancy, is destined to fail. While placing cocaine-using mothers in jail satisfies a public sense of order in our society, it promises little to decrease problems of the fetus and neonate. Experience has shown that the mothers continue to seek substances while incarcerated, and that habitual users shun prenatal care for fear of arrest. One powerful threat to pregnancy is absent or delayed prenatal care, and substance abusers already are the most frequently encountered unregistered patients on our delivery floors. Nonpunitive ap-

proaches, including the offering of treatment options to pregnant women with cocaine and other substance problems, is much more likely to be effective. Every prenatal care provider should take a thorough substance (including alcohol) history, and offer treatment to those women so identified.

Prevention

Emphasis here is on the addicted mother yet acute perinatal complications can occur when a pregnant woman first tries cocaine or uses it only occasionally. In addition, all addicts start out as occasional users. Therefore, prevention must be considered vital to treatment.

The key to prevention is education. Programs in health care facilities, schools, and the media must inform women who are not yet pregnant about cocaine and other substance risks during pregnancy.

The key to prevention is education. Programs in health care facilities, schools, and the media must inform women who are not yet pregnant about cocaine and other substance risks during pregnancy. While the "hard core" cocaine user is less likely to respond to such efforts, the large number of "occasional" or "potential" users may avoid endangering their unborn children. Just as the use of over-the-counter drugs, tobacco and alcohol during pregnancy seems to have diminished thanks to educational efforts in recent years, we must hope that the same will be true of cocaine and other illicit substances.

References

- Moore TR, Sorg J, Miller L, Key T, Resnik R: Hemodynamic effects of intravenous cocaine on the pregnant ewe and fetus. *Am J Obstet Gynecol* 1986;155:883-888.
- Woods JR Jr, Plessinger MA, Clark KE: Effect of cocaine on uterine blood flow and fetal oxygenation. *JAMA* 1987;157:957-961.
- Creigler LL and Mark H: Special report: Medical complications of cocaine abuse. *N Engl J Med* 1986;315:1495-1500.
- Mercado A, Johnson G Jr, Calver D, Sokol RJ: Cocaine, pregnancy, and postpartum intracerebral hemorrhage. *Obstet Gynecol* 1989;73:467-468.
- Henderson CE, Torbey M: Rupture of intracranial aneurysm associated with cocaine use during pregnancy. *Am J Perinatol* 1988;5:142-143.
- Acker D, Sachs BP, Tracey KJ, Wise WE: Abruptio placentae associated with cocaine use. *Am J Obstet Gynecol* 1983;146:220-221.
- Chasnoff IJ, Burns WJ, Schnoll SH, Burns KA: Cocaine use in pregnancy. *N Engl J Med* 1985;313:666-669.
- Bingol N, Fuchs M, Diaz D, Stone RK, Gromisch DS: Teratogenicity of cocaine in humans. *J Peds* 1987;110:93-96.
- Oro AS, Dixon SD: Perinatal cocaine and methamphetamine exposure: maternal and neonatal correlates. *J Peds* 1987;111:571-578.
- Hadeed AJ, Siegel SR: Maternal cocaine use during pregnancy: effect on the newborn. *Pediatrics* 1989;84:205-210.
- Chasnoff IJ, Griffith DR, MacGregor S, Dirkes K, Burns KA: Temporal patterns of cocaine use in pregnancy: perinatal outcome. *JAMA* 1989;261:1741-1744.
- Keith LG, MacGregor S, Friedell S, Rosner M, Chasnoff IJ, Sciarra JJ: Substance abuse in pregnant women: recent experience at the Perinatal Center for Chemical Dependence of Northwestern Memorial Hospital. *Obstet Gynecol* 1989;73:715-720.
- MacGregor SN, Keith KG, Chasnoff IJ, Rosner MA, Chisum GM, Shaw P, Minogue JP: Cocaine use during pregnancy: adverse perinatal outcome. *Am J Obstet Gynecol* 1987;157:686-690.
- Chouteau M, Namerow PB, Leppert P: The effect of cocaine abuse on birth weight and gestational age. *Obstet Gynecol* 1988;72:351-354.
- Neerhof MG, MacGregor SN, Retzky SS, Sullivan TP: Cocaine abuse during pregnancy: peripartum prevalence and perinatal outcome. *Am J Obstet Gynecol* 1989;161:633-638.
- Little BB, Snell LM, Klein VR, Gilstrap LC: Cocaine abuse during pregnancy: maternal and fetal implications. *Obstet Gynecol* 1989;73:157-160.
- Frank DA, Zuckerman BS, Amaro H, Aboagye K, Bauchner H, Cabral H, Fried L, Hingson R, Kayne H, Levenson SM, Parker S, Reece H, Vinci R: Cocaine use during pregnancy: prevalence and correlates. *Pediatrics* 1988;82:888-895.
- Cherukuri R, Minkoff H, Feldman J, Parekh A, Glass L: A cohort study of alkaloidal cocaine ("crack") in pregnancy. *Obstet Gynecol* 1988;72:147-151.
- Mitchell M, Sabbagha R, Keith L, MacGregor S, Mota JM, Minoque J: Ultrasonic growth parameters in fetuses of mothers with pri-

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Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors. Its effect on blood pressure, if any, would be to lower it, however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

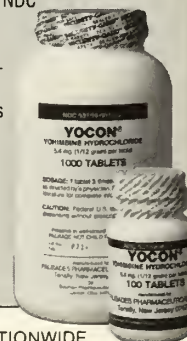
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon[®] 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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- mary addiction to cocaine. Am J Obstet Gynecol 1988;159:1104-1109.
- 20 Chasnoff IJ, Bussey ME, Savich R, Stack CM: Perinatal cerebral infarction and maternal cocaine use. J Peds 1986;108:456-459.
 - 21 Chavez GF, Mulinare J, Cordero JF: Maternal cocaine use during early pregnancy as a risk factor for congenital urogenital anomalies. JAMA 1989;262:795-798.
 - 22 Madden JD, Payne TF, Miller S: Maternal cocaine abuse and effect on the newborn. Pediatrics 1986;77:209-211.
 - 23 Doberczak TM, Shanzer S, Senie RT, Kandall SR: Neonatal neurologic and electroencephalographic effects of intrauterine cocaine exposure. J Peds 1988;113:354-358.
 - 24 Chasnoff IJ, Burns KA, Burns WJ: Cocaine use in pregnancy: perinatal morbidity and mortality. Neuro Toxicol and Teratol 1987;9:291-293.
 - 25 Dixon SD, Coen R, Crutchfield S: Visual dysfunction in cocaine-exposed infants. Pediatr Res 1987;21:359A.
 - 26 Schneider JW, Chasnoff IJ: Cocaine abuse during pregnancy: its effects on infant motor development — a clinical perspective. Top Acute Care Trauma Rehab 1987;2:59-65.

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ERRATUM

The author, Alan A. Wartenberg, MD, of the paper, "Detoxification of the Chemically Dependent Patient," *Rhode Island Medical Journal*, December 1989, Vol 72, wishes to correct two dosage figures appearing in Table 2 — Hypnotosedative Drugs on page 454 of that same issue. The equivalent dose for Chlordiazepoxide should be 25 mg instead of 10 mg. The equivalent dose for Clorazepate should be 3.75 mg instead of 7.5 mg.

Adolescent Substance Use and The Role of the Primary Care Provider

Suzanne Riggs, MD
Anthony J. Alario, MD

A disturbing current trend is that children are beginning drug use at an earlier age.

Magnitude of the Problem

In past decades, American teenagers often experimented with "legal" substances such as alcohol and cigarettes but rarely used illicit drugs. By 1985, however, 61% of high school seniors admitted to at least experimental use of illicit drugs. The number of adolescents who use "legal" drugs has also risen. About two-thirds now use alcohol and one-third smoke cigarettes on a regular basis (Fig 1).¹

Marijuana is the most widely used illicit drug among young people although stimulants (such as amphetamines and cocaine) are also popular. While adolescent cocaine use is widely pub-

licized, amphetamine and inhalant drug use are also prevalent.

A disturbing current trend is that children are beginning drug use at an earlier age. In 1986 almost one-half of high school seniors reported using an illicit substance by the 10th grade, compared to one-third in 1975.² It is noteworthy that school drop-outs are not included in these use data.

Longitudinal studies suggest that drug use follows a predictable sequence.³ If a person uses one drug, he is more likely to use other drugs. Teenagers usually begin with the "gateway" legal drugs, alcohol or tobacco, progress to marijuana, and may eventually go on to use other illicit drugs or combinations of drugs. About 50% of those who try marijuana eventually progress to more potent psychoactive drugs. Few cocaine and heroin users have not previously used alcohol, tobacco and/or marijuana. For young women, smoking cigarettes at an early age seems important in subsequent involvement in drug use. For young men, marijuana use is a strong predictor of greater drug involvement.⁴

Whether and when youngsters progress to other drugs is quite variable. Some adolescents prog-

ress rapidly to a wide variety of drugs, others use a given substance a few times and then quit. For the most part, those who have not begun to experiment with alcohol, cigarettes, and illicit drugs before the ages of 18 to 21 are unlikely to do so. By the age of 21, the proportion of those who use illicit drugs usually decreases.

Cocaine, however, shows a striking exception to these patterns. In 1986, its use among teenagers was at an all-time high. About 17% of high school seniors questioned in the National Drug Survey reported having used cocaine at some time. 12% reported using cocaine in the past year; 6.7% reported using cocaine in the past 30 days. Daily use of cocaine among high school seniors doubled from 1983 (0.2%) to 1986 (0.4%).² Longitudinal studies tracking teenagers into their 20s indicated that the frequency of cocaine use increases with each successive year after high school graduation and continues into early adulthood.² There is some recent evidence, however, to suggest that a gradual decline in frequent cocaine use among adolescents and young adults has finally begun.¹

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Experimental vs. Regular Use: Four Phases of Chemical Dependency

Most adolescents use drugs with their peers in social settings, often supplied and invited by friends "to see what happens" or to "learn about being high." Many youngsters experiment with cigarettes, alcohol, or marijuana and never go on to use these substances again. Some adolescents, however, continue experimental use until "the high" attracts them to begin seeking their own supply of drugs to share at social occasions and to use alone. During this phase, the teenager learns which drugs offer which effects while seeking mood changes through drug use — perhaps as a means of self-medicating for adolescent anxieties and/or depression. Ordinarily, youngsters who actively seek, buy and use their own drugs or alcohol prefer a "user" peer group. "Straight" friends are left behind.

Ordinarily, youngsters who actively seek, buy and use their own drugs or alcohol prefer a "user" peer group. "Straight" friends are left behind.

Eventually, drugs become crucial for coping and coping seems impossible or difficult without drugs to modulate emotional stresses. The user becomes preoccupied with thoughts about the "next high." Finally, use becomes compulsive, the high is no longer euphoric and drug use becomes a way to prevent the unpleasant effects of withdrawal. This last stage is rarely seen in adolescents.

Risk Markers for Problem Drug or Alcohol Use

Pioneering work by Jessor has identified factors that increase the

likelihood of drug abuse, delinquency and other behavior problems during adolescence.⁵ These factors include a family history of alcoholism, exaggerated family dysfunction, and poor family management practices with inconsistent rules for behavior and inconsistent reactions to the child's behavior. Early antisocial behavior and childhood conduct disorders with aggression, hyperactivity, inattentiveness, impulsiveness, and defiant acting out also have been related to later teenage drug use.

In general, youngsters at risk are those who underachieve in mid to late elementary school and place little value on education. Belonging to a drug-using peer group is a major contributing factor for teen drug use. Youngsters who are tolerant of deviant or antisocial behavior, are alienated, or do not place any value on religion, are also at special risk for using drugs. Adolescents with early, promiscuous sexual activity or eating disorders — especially bulimia, are also potentially likely to be substance users.^{5,6,7} In addition, we have found that adolescents with a prior history of physical abuse are at a substantially increased risk for drug use compared to nonabused peers.⁸

Role of the Primary Care Provider

The vast majority of teenagers in the United States who have used drugs do so by the time they reach the 12th grade. Therefore, it is imperative that providers of health care to children and adolescents become comfortable in evaluating their patients for substance-use. At the very least, physicians should be able to identify the adolescent with a significant substance-use problem. Providers must also recognize the need to screen for substance-use by di-

rect questioning when chronic complaints of frequent injuries, fatigue, abdominal pain, chest pain, headaches, coughing and sore throat present. In general, a standard physical exam, routine laboratory tests and the "toxic screen" will not be helpful for diagnosing adolescent substance use during an office visit. The time necessary to perform a comprehensive evaluation and provide education, particularly related to substance-use, is substantial. Therefore, health professionals should schedule additional time to explore this important area, especially when routine visits are infrequent as in the adolescent years.

... identified factors that increase the likelihood of drug abuse ... include a family history of alcoholism, exaggerated family dysfunction, and poor family management practices with inconsistent rules for behavior.

The adolescent should be interviewed in private, to reassure the patient that the discussion is confidential and that any information discussed will not, under most circumstances, be made available to his/her parents without permission. The physician should let teenagers know that he genuinely cares about them, and that knowing details about their life style and habits helps provide better medical care. This approach places the topic of substance use in the context of concern for the patient's health: "I would like to know a little about you, and about what you do in this regard, because it is important to your health." It is also important to be non-judgmental and to introduce the topic of drug and

alcohol use in a non-threatening way: "I know a lot of kids your age use drugs and alcohol," or "Most teens I know wonder if smoking marijuana interferes with good driving judgment the way that beer, wine and liquor does." Following some general discussion, it is important to assess the risk for drug and alcohol use in a very firm and direct way.

During the interview, a teenager who feels that his substance-use is in danger of discovery will resort to defenses to protect or deny problems. The interviewer should recognize these protective strategies, acknowledge their existence, and return to the interview. The frightened and angry adolescent, for example, may resist in engaging in the interview by refusing to answer any questions. By responding in a warm and empathetic way ("You seem quite upset about being here today, I can understand your not wanting to come") the interviewer can gain respect and acknowledge that the adolescent is in fact uncomfortable. It will sometimes be necessary to question any factual misinformation as well as to let the patient know when you notice inconsistencies in the history. It is often necessary to gain a general understanding of the social environment of the adolescent. In this regard, family and peer relationships are explored as well as areas of school performance, leisure activities, and a general assessment of the patient's self esteem.

Based on currently available data, we have identified five questions which could be used in "screening" adolescent patients for risk of substance use. The questions have the acronym "RAFFT."⁹

1. Do you drink or use drugs to *RELAX*, feel better about yourself, or to fit in?

2. Do you ever use drugs when you are by yourself or *ALONE*?
3. Do you or any of your closest *FRIENDS* drink or use drugs?
4. Does a close *FAMILY* member have a problem with alcohol or drug use?
5. Have you ever gotten into *TROUBLE* from drinking or drug use (ie, skipping school, bad grades, trouble with the law or parents)?

For those patients who answer "no" to all of the questions on the RAFFT, it is important to determine the potential for use by asking questions such as "Have you ever been tempted to try alcohol or drugs because of your friends?" or "If your friends offer you alcohol or drugs, would you try them?" "Why or why not?" The physician should express concern about health problems related to alcohol and drug use, and allow patients to describe their understanding of the problems. In addition, it might be necessary to correct any misunderstandings, and to provide valid facts about substance use either through conversation or by printed material such as pamphlets in the waiting or exam rooms. The health provider should reinforce any positive attitudes expressed by the patient regarding the avoidance of alcohol or drugs, and suggest additional strategies for avoiding drug use.

A positive answer to any of the RAFFT questions may indicate a potential for a serious problem. In this situation, asking for further details may pave the way to allowing patients to communicate concern. For example, subsequent questions may include the following: "Do you drink regularly?" "About how often?" or "Do you ever drink specifically to

'pass-out'?" The context in which the drug use occurs can offer clues to treatment approaches. Does the use occur at social functions with friends, or when they are alone? Some assessment of dependence is important: "Do your social activities always involve alcohol or drug use?" "Do you buy your own alcohol or drugs?" Finally, information about the psychosocial consequences of substance use should be obtained. "Have you gotten into trouble because of drugs?" "Do your parents suspect that you drink or take drugs?"

If a person uses one drug, he is more likely to use other drugs. Teenagers usually begin with the "gateway" legal drugs, alcohol or tobacco, progress to marijuana, and may eventually go on to use other illicit drugs or combinations of drugs.

Table 1 provides guidelines for the primary care physician in deciding when to personally manage or to refer the adolescent who admits to using drugs. Most health care providers are not in the position to assume the responsibility for the actual treatment of an adolescent who is in need of significant therapy. However, providers can be an important conduit for providing information, ensuring effective communication and making an appropriate referral for more detailed evaluation and treatment. In approaching these patients, the physician should allow the patient to describe his understanding of the problem first. Then by summarizing the information disclosed during the evaluation, the physician can provide a clear statement to the adolescent about his/

TABLE 1
CRITERIA FOR TREATMENT AND REFERRAL OF THE ADOLESCENT
SUBSTANCE USER*

FOLLOW-UP CARE BY PRIMARY CARE PHYSICIAN

Physician/family practitioner knowledge in these areas
 Drug use intermittent, experimental, and not unusual for age/sociocultural group
 No significant psychopathology
 Function in educational, social, or vocational sphere unimpaired
 Reasonable progress in developmental tasks
 No antisocial behavior

REFERRAL TO SPECIALIZED PRACTITIONER

Lack of experience or uncertainty on part of the primary physician
 Significant drug abuse (frequent/regular, major life concern)
 Psychopathology requiring evaluation and care
 Impaired function in educational, social, legal, or vocational sphere
 In certain instances (i.e., when a specialized unit is available) evaluate on an inpatient basis.

REFERRAL TO INPATIENT DRUG TREATMENT PROGRAM

Compulsive drug abuse
 Impaired function in educational, social, legal, or vocational sphere
 Imminent danger to physical or mental health of patient
 Persistent antisocial behavior
 Failure of outpatient treatment
 Psychopathology requiring behavior control, medication, or both

* Adapted from Millman RB: Treatment and modalities, in Litt IF (ed): Adolescent Substance Abuse, Report of the 14th Ross Roundtable on Critical Approaches to Common Pediatric Problems. Columbus, OH, Ross Laboratories, 1983, pp 63-64.

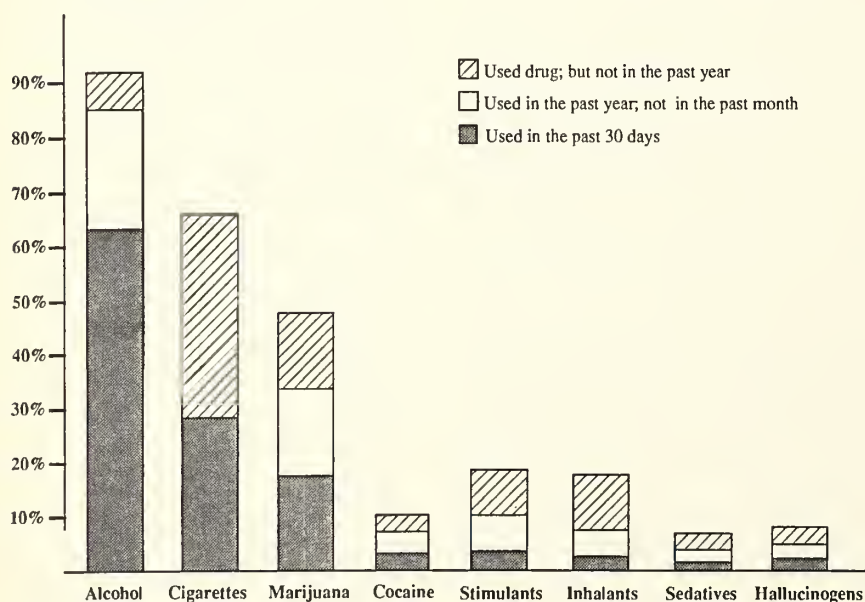
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her problem substance use and outline how drugs or alcohol harm health and lead to dysfunction. Thus, the physician provides concrete medical and psychosocial evidence of a problem. The physician should display empathy and genuine concern "I am very worried about you and concerned about your substance-use."

The provider must stress the need to enlist support of the patient's parents to address a serious substance-use problem. The provider may state to the adolescent: "I would like to have your permission to talk to your parents about this. It is important to involve them because, to provide the best treatment for your problem, we will need their support." The primary care provider should assume the responsibility for acting as an intermediary between patients and their parents. Finally the provider will have to negotiate for follow-up appointments, to discuss details of drug use further. If a referral is to be made to an agency which deals with drug and alcohol problems in adolescents, it is important that the teenager and the family do not perceive the referral as a rejection by the primary care physician. Personalize the referral process by identifying a therapist or treatment program that the physician knows well and recommends. It is also important to state that you will continue to be the youngster's physician for this and other health problems. It is advisable to schedule a follow-up appointment after the first treatment session in order to find out how the adolescent is doing, and to make sure that appointments have been kept.

As with any medical problem, prevention is better than providing a cure. Key prevention efforts are aimed at helping young people survive the vulnerable years without using drugs or to delay their use. Strategies to avoid sub-

High School Seniors Class of 1988
Prevalence



stance-use should be a part of "anticipatory guidance" provided by pediatricians and other health care workers at each routine medical visit for any school-age child. The information should always be provided in a developmentally-appropriate context and show clearly how drug use relates to overall health. Finally, concerned health professionals collaborating with parents, and community agencies, assure that drug prevention efforts have a child and family oriented focus.

References

- ¹ Johnston LD, O'Malley PM, & Bachman JG (1989). *Drug Use, Drinking, and Smoking: National Survey Results from High School, College and Young Adult Populations*. (ADM) 89-1638. Rockville, MD: U.S. Department of Health and Human Services, NIDA.
- ² Johnston LD, O'Malley PM & Bachman JG (1988). *Illicit drug use, smoking, and drinking by America's high school students, college students, and young adults 1975-1987*. (ADM) 89-1602. Rockville, MD: U.S. Department of Health and Human Services, NIDA.
- ³ Kandel DB (1975). Stages in adolescent involvement in drug use. *Science*, 190, 912-914.
- ⁴ Kandel DB & Logan JA (1984). Patterns of drug use from adolescence to young adulthood: I. Periods of risk for initiation, continued use, and discontinuation. *American Journal of Public Health*, 74, 660-666.
- ⁵ Jessor R (1987). Problem-behavior theory, psychosocial development and adolescent problem drinking. *British Journal of Addiction*, 82 331-342.
- ⁶ Klitzner M, Schwartz RH, Gruenewald P & Blasinsky M (1987). Screening for risk factors for adolescent alcohol and drug use. *American Journal of Diseases of Children*, 141, 45-49.
- ⁷ Newcomb MD, Maddahian E & Bentler PM (1986). Risk factors for drug use among adolescents: Concurrent and longitudinal analyses. *American Journal of Public Health*, 76 (5), 525-531.
- ⁸ Riggs S, Alario A, McHorney C; Health Risk Behaviors and Attempted Suicide in Adolescents who Report Prior Maltreatment. *Journal of Pediatrics* (In Press).
- ⁹ Riggs S, Alario A, Adolescent Substance Use. Module in The Project ADEPT Curriculum for Primary Care Physician Training, eds Dube C, Goldstein M, Lewis DC, and Zwick WR, Brown University 1989.

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The Physician's Role in Rehabilitating Chemically Dependent Patients

John Femino, MD
William Griffith, MD

Physician involvement and leadership lagged until dependency problems were understood as a primary disorder, with biological as well as psychological and social factors.

Our society has always had mixed feelings and attitudes towards psychoactive substances. Alcohol, for example, is legal, taxable, pleasurable, ceremonial, but also may become painful, addicting, unhealthy and criminal. The dual potential of psychoactive substances (pleasure and pain) shapes our societal response. The physician's role in treating these problems has been similarly affected with ambivalence. Historically, physicians have been skilled at treating medical complications of heavy drinking; however, they have had little involvement in addressing the

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drinking problem itself. Often alcoholics who come out of the closet and go public with their stories, credit their success to someone other than their doctors, if not blaming them for misdiagnosis and over-medication.

Stories persist of doctors treating anxiety and gastritis without ever taking a drinking history, often referring patients to a psychiatrist who also would ignore it. Most physicians lacked training and experience in treating the underlying addictive disorder. Further, chemically dependent patients are not easy to diagnose, may not assume a traditional "sick" role and exhibit symptoms non-specific enough to masquerade as another set of problems. Patients' denial, minimization and unreliability can generate such frustration and negative attitudes that most physicians find it easier to act like unquestioning technicians than diagnosticians and therapists.

Historical Development of Addiction Specialty

Not understanding the dynamics of chemical dependency seeds negative attitudes in both care-

givers as well as the patients. Fortunately, this historical ostrich-like physician's posture is rapidly changing. Physician involvement and leadership lagged until dependency problems were understood as a primary disorder, with biological as well as psychological and social factors. In the 1970s and 80s public sentiment began to influence funding for research, education and treatment. NIAAA and NIDA created the Career Teacher program, which provided funding to over 60 medical

ABBREVIATIONS USED:

AA: Alcoholics Anonymous
AMERSA: Association for Medical Education and Research in Substance Abuse
ASAM: American Society of Addiction Medicine
GGTP: gamma globulin, total protein
LSD: lysergic acid diethylamide
MCV: mean corpuscular volume (erythrocyte)
NA: Narcotics Anonymous
NIAAA: National Institute for Alcohol Abuse and Alcoholism
NIDA: National Institute for Drug Abuse

schools to support faculty to develop and implement drug and alcohol abuse curricula. Its successor organization, the Association for Medical Education and Research in Substance Abuse (AMERSA) represents over 1,500 members and significantly influences the direction of medical education for both medical students and practicing physicians. Growing numbers of interested physicians were instrumental in forming such professional organizations as the American Society of Addiction Medicine (ASAM). This 3,600-member international organization seeks to further knowledge and skill, has developed a certification examination, and is now exploring a separate medical specialty status.

Developing a separate medical specialty of addiction medicine has its challenges, as these problems are cross-disciplinary and intersect specialties. Although most chemically troubled patients remain unidentified in primary care physician practices, some practitioners cannot accept a role to intervene. Overcoming negative attitudes and stereotypes of chemical dependency requires a new level of contact, communication and cooperation between specialist and generalist. Nationally, this collaboration starts when addiction specialty groups assist in identifying and developing minimum knowledge and skills that general practitioners need in their respective primary care discipline. Copies of these documents are available from the primary care discipline organizations, ie, the American Colleges of pediatrics, internal medicine, family medicine and psychiatry.

Assessing Addiction Problems

Physicians become involved with chemically dependent patients first in the assessment process.

Patients are frequently in a high state of denial, often forced into assessment by threats of divorce, imprisonment or loss of job. Usually patients are angry and full of self-pity. They feel that others are picking on them and that their true problem is a spouse, or the police or a boss and not alcohol or drugs. They minimize the extent of their drinking and/or drug use and will frequently try to co-opt the physician to side against spouse, boss, etc. During assessment, our goals are to 1) identify a substance abuse problem, 2) evaluate the severity of that problem and 3) offer the appropriate treatment for the problem.

Surprisingly, discovering a problem is next to impossible if only the patient is interviewed.

Sometimes patients freely admit that a drinking or drug problem requires treatment, but this is unfortunately rare. More often the patient tries to prove there is no problem or to hide symptoms. Nevertheless, the starting place is with the patient. We assess the patient by probing all important areas of life as it pertains to alcohol and drug use.

Key questions to identify a problem include alcoholism in the family, prescription and over-the-counter drug use (in addition to those for which a patient presents at the office) and attempts to control drinking/drug use as a tell-tale sign. Efforts to control include quitting or limiting for periods of time to prove that one has control, changing alcohol types

Table 1

Effects of Substance Abuse on Life Functioning	
Social	Embarassing Incidents Drinking Alone Financial Problems
Family	Family Discord Covering Up Problems Fear of Confronting Drinker
Emotional	Depression Suicidal Ideation Anxiety
Legal	Arrests for DWI Restraining Orders Protective Custody
Job	Absenteeism Substance Use at Work Job Warnings/Loss Declining Performance
Health	Accidents/Trauma Drug Specific Organ Damage Unexplained Treatment Failure Abstinence Syndromes

or patterns of drug use and developing rules and restrictions for drinking or drugging.

After gathering this information, a physical examination should be performed, with special emphasis on alcohol and drug-related abnormalities. High blood pressure or pulse with a fine tremor may indicate alcohol withdrawal syndrome. Breath alcohol is certainly significant. Carefully inspect nasal membranes for signs of cocaine damage. We have noted that many cocaine snorters use only one nostril, which appears friable and eroded, while the other appears perfectly normal. Since dental neglect is common among alcoholics and addicts, inspect teeth carefully. Check the body for signs of liver impairment such as spider angiomas, jaundice, liver enlargement, nodularity of the liver, ascites and peripheral edema. Evaluate the nervous system carefully for signs of cerebral and cerebellar atrophy and peripheral neuropathy. Finally, inspect the skin for bruising (alcoholics and addicts fall frequently and are often unaware of large bruises on their bodies) or needle tracks (most often in the antecubital area but also concealed in tattoos or under watch bands).¹

Next, do a laboratory examination. Specific indicators of alcohol problems are increased MCV, unexplained anemia and/or thrombocytopenia, elevated SGOT, SGPT (particularly if the SGOT > SGPT), elevated uric acid, elevated GGTP and unexplained, elevated triglyceride levels. Specific indicators of drug problems are signs of malnutrition such as decreased albumin and lipid levels, elevated liver enzymes (SGPT > SGOT), positive tests for current or past Hepatitis B, and positive urine drug screens for the drugs and their metabolites. To be useful, the urine tests

should be obtained in front of a witness to eliminate specimen tampering. Most drugs remain in the urine for two to three days after last use. Exceptions are cocaine, detectable only for 12 to 24 hours after use (although the cocaine metabolite, benzoylecgonine, is present for three days after last use). LSD, which is present only briefly; and marijuana (THC), present in urine for up to one week after use of one joint and up to 30 days in regular heavy users (3 or more joints per day).²

Positive findings (from physical examination and laboratory evaluations) can be very significant and useful in confronting a patient's denial.

If physical examination and laboratory evaluations are normal, they have limited usefulness in ruling out a suspected substance abuse problem. However, positive findings can be very significant and useful in confronting a patient's denial. All information is now brought together and shared with the patient in a repeat appointment. Sometimes this evaluation clearly indicates a problem and the patient can be confronted and treatment recommendations outlined. Frequently, however, uncertainty still remains regarding the presence of an alcohol or drug problem. Now, it is necessary to gather more information from those who know the patient best — his family and even, on occasion, his employer. The patient may resist or refuse to allow those people to be questioned, itself often a strong problem indicator. Usually though, the patient will permit you to contact these people. At this point, we again probe areas of life functioning, but with the spouse or significant other answering.

Frequently, if an alcohol or drug problem exists, a marked discrepancy emerges between the patient's story and the significant other's reports. We have noticed this particularly when evaluating teenagers.

After this new information is gathered the patient can then be confronted again. We use a supportive, non-threatening approach — not trying to bludgeon the patient into acknowledging a problem. We want a patient to know that we know a problem exists and that we have solutions to the problem if he seeks them. Following this confrontation, the patient may be willing to seek treatment, but he may not. If not, we leave the door open to return if he feels he needs help in the future. Frequently, patients come back and seek help later.

Rehabilitation

If, after the assessment, the patient is willing to enter treatment, rehabilitation begins. Its goal is to break through the patient's denial so that he can confront and accept his addiction and willingly enter into treatment and/or self-help programs such as Alcoholics Anonymous. Triggers for relapse are explored including the stability of the patient's living arrangements and possible changes to enhance recovery. Rehabilitation programs are highly structured using group and individual counseling, alcohol and drug lectures, drug-free leisure activities, and daily in-house AA and NA meetings. Trained counselors, nurses, psychologists, clergy, and physicians work closely together as a team. Intensely involved in the rehabilitation process, the physician confronts the patient's denial regarding physical damage from alcohol or drugs, helps develop a Master Treatment Plan and usually directs the treatment planning process. The physician

supervises how nursing and counseling staff interact with the patient and lends authority to their efforts. The physician directs treatment of a patient's coexisting medical problems, motivating patients to use non-medical means instead of drugs for stress, anxiety, insomnia and pain. The physician also helps develop the discharge plan, including referral for appropriate ongoing counseling.

Pharmacotherapy of Addiction

Once detoxified, a patient may need Antabuse (disulfiram) therapy. Antabuse helps a patient "think twice" about daily temptation to drink since he risks becoming seriously ill if he drinks on Antabuse. It also can reduce craving since the patient makes one "big" decision not to drink when he takes the pill each day. This can stiffen his resistance to further impulses. It makes abstaining easier especially for those whose work or social lives involve alcohol.³ A somewhat similar medication, Trexan (naltrexone), exists for narcotic dependence. Naltrexone is a non-addicting narcotic receptor blocker. For the patient taking naltrexone, narcotics have no effect, obviously helpful in abstaining. Major drawbacks are the drug's tendency to produce or enhance depression in recovering addicts and the inability to use narcotics for pain if injury should occur.

Common Problems of Early Recovery

Bouts of anxiety, depression and insomnia are common in early recovery whether the person is recovering from alcohol or drugs. These problems usually fix themselves with time; medication is not necessary. Unfortunately, physicians often prescribe benzodiazepines for these problems. Because they frequently re-ignite

craving that can lead to relapse, benzodiazepines and other mood-altering drugs are very dangerous for the recovering person. The addiction specialist uses the prescription pad very sparingly. To help the patient deal with life's problems without self-medicating, only medically necessary drugs need be prescribed. Commonly rehabilitation programs restrict use of Tylenol (acetaminophen) and aspirin, applying non-chemical solutions to manage everyday complaints.

Relapse

Inevitably, some recovering patients relapse back to alcohol or drug use. Our goal is to stop the relapse as soon as possible to get the patient back into recovery. Short-term hospital detoxification and stabilization may be necessary to interrupt the relapse successfully. Once the relapse has ended the patient and physician can explore the cause for the relapse and restructure an after-care plan to avoid future relapses. The addiction medicine specialist views relapse in much the same way as the diabetologist — an unfortunate occurrence from which much can be learned to help the patient better cope with his disease in the future.

Continuity of Care Issues

Despite advances, fewer than 10% of all referrals into inpatient alcoholism and chemical dependency rehabilitation programs come from the patient's primary care physician. Furthermore, many patients admitted to treatment do not want their physician notified, fearing disapproval, abandonment or a threat to their relationship.⁴ Changing this situation requires a mutual sharing of information and support. Knowing how treatment works is paramount to a practicing physician's ability to educate patients

and provide sound advice on available and appropriate treatment options.

Knowing how treatment works is paramount to a practicing physician's ability to educate patients and provide sound advice on available and appropriate treatment options.

Although it is often difficult to get permission, every patient's primary care physician should be notified that the patient is in a substance abuse treatment program — with direct doctor-to-doctor contact. Most primary care physicians welcome the contact and are receptive to the consultants' advice. If the patient's physician resists treating the patient because of frustration, lack of patient participation, family or financial problems, the addiction specialist helps to assess the reality of these concerns and attempts to break down superficial barriers to ongoing treatment.

The addiction specialist may discuss with the primary care physician ongoing problems that may require exposure to potentially addicting drugs, such as patients with co-existent anxiety disorders, other mood disturbances or chronic painful conditions. If medication is necessary, it should be sparingly given without generating unnecessary fear of re-addiction. The addiction specialist can take advantage of the opportunity to provide ongoing assistance and consultation to the primary care physician after the patient's discharge from inpatient care, especially if the patient is going to receive outpatient substance abuse treatment. In this manner addiction specialists can avoid being perceived as taking over the patient's total care from the primary physician. Further,

once such relationships exist, the primary care physician may then receive new patient referrals from chemical dependency programs.

Conclusion

From a historical perspective, the best thing about today's physician role in the rehabilitation of the chemically dependent patient is the fact that his/her role exists at all. Treatment efforts that excluded physician participation are waning as the knowledge base of all physicians develop, led by addiction medicine specialists and their respective organizations. Treating the primary addiction problem is now as legitimate a focus as treating the medical symptoms used to be. Specialization, however, cannot operate effectively outside the mainstream of medical care since addiction involves a complex of inter-related people, problems and

institutional responses. Free-standing programs can bridge the geographic gaps that often separate specialists from their medical colleagues — by drawing the primary care physician into the treatment team. Contact, communication and cooperation are the links that can create a more effective treatment triangle. Exposure to recovering patients within the context of a guided recovery process will nurture appropriate interest and enthusiasm and, in itself, be the best teacher known.

References

- ¹ Eckardt MJ, Harford TC, Kaebler CT, et al. Health hazards associated with alcohol consumption. JAMA 1981;246:648-666.
- ² Schwartz Richard H and Hawks Richard L. Laboratory Detection of Marijuana Use. JAMA 1985;254(6):788-792.
- ³ Kwentus J, Major LF. Disulfiram in the treatment of alcoholism. A review. J Stud Alcohol 1979;40:428-446.
- ⁴ Clark WD. Alcoholism: blocks to diagnosis and treatment. Am J Med 1981;71:275-286.

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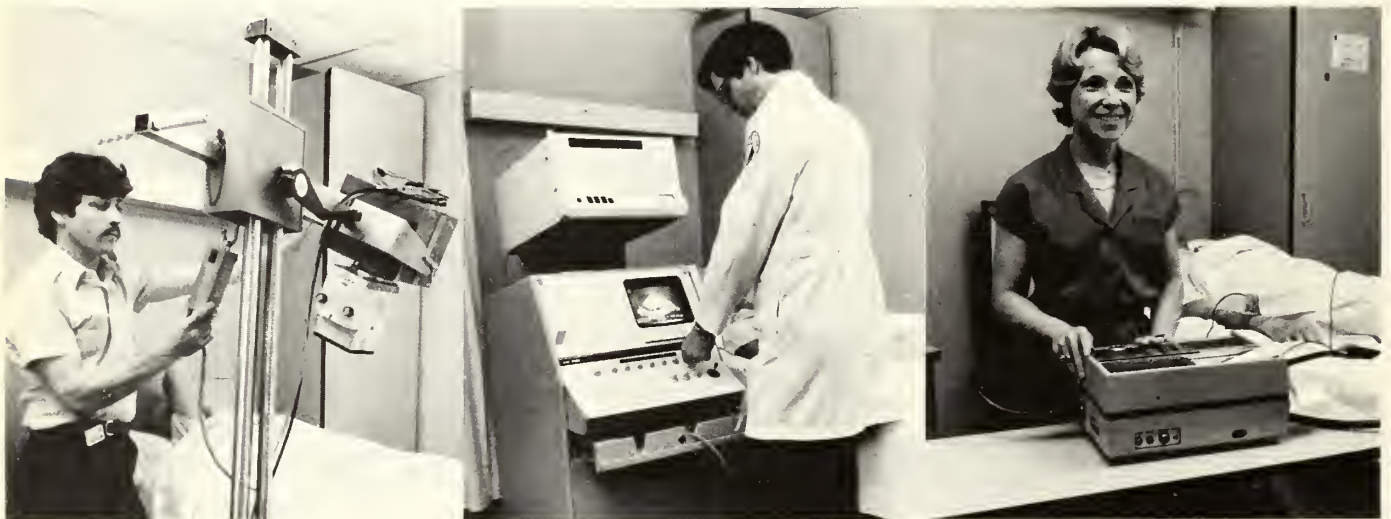
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Cocaine Abuse and Dependence

Robert M. Swift, MD, PhD
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Many physicians and practitioners who advocated cocaine for others (between the years of 1884-1900) developed a significant dependence on the drug themselves.

Cocaine, or benzoylmethylecgonine, is an alkaloid drug extracted from the leaves of several species of shrubs *Erythroxylon coca*, which grow naturally on hillsides of the Andes Mountains in Peru and Bolivia. In the past two decades, usage of cocaine has increased to epidemic proportions and patterns of cocaine use have changed from intranasal "snorting" of cocaine hydrochloride powder to smoking or intravenous injection of more potent cocaine "freebase." Freebase cocaine is now widely available in a product called "crack," which

is extremely potent, inexpensive and easily distributed. Crack is most-often self-administered by smoking, usually by adding a small piece to a burning cigarette or heated pipe and inhaling the vapor.

This article provides basic information on the pharmacology and physiology of cocaine-use disorders and on the identification and treatment of cocaine abusers.

History of Cocaine Use

The use of cocaine has a long history in the New World. The first archaeological evidence of coca chewing in Peru has been dated at 3000 BC.¹ Cocaine was brought to the Old World in the 18th century by explorers, but remained a novelty studied by a few pharmacologists and physiologists until the latter part of the 19th century.

The current explosion in cocaine use in this country is actually not the first such occurrence. Between the years of 1884-1900, a first wave of extensive cocaine use occurred in the US and Europe. Two papers, one presented by Koller in 1884 in Heidelberg and a second presented

by Halstead in 1885, reported the anesthetic properties of cocaine.^{2, 3} The use of cocaine spread rapidly after these reports; physicians of the time touted the drug for hay fever, asthma, sciatica, tuberculosis, and the common cold. Parke-Davis promoted the drug in an extensive ad campaign for treatment of alcoholics and opium addicts.

Many physicians and practitioners who advocated cocaine for others developed a significant dependence on the drug themselves. William Halstead and Sigmund Freud developed well publicized impairments from addiction to the drug. In 1893, Mattison, medical director of the Brooklyn Home for Habitues, wrote in the *New York Medical Record* detailing the cases of 17 patients under his care for cocaine habits; 10 were physicians.

Cocaine also appeared in patent medicines of the time, including the famous "Vin Mariani" and the less well known but equally effective Binney's "Catarrh Snuff" (containing 2.5% cocaine). In 1898, a case of cocaine snuff addiction was reported in the *Boston Medical and Surgical Journal*, now the *New England*

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Journal of Medicine. A patient had been using large amounts of cocaine-containing snuff daily, running up bills of \$600 per day.⁴

Between 1893 and 1990, many reports published in the medical literature described cocaine patients who became incoherent, shouting, singing, wrecking furniture, and in one case, physically attacked the surgeon. There were occasional reports of deaths preceded by convulsions, asystole or respiratory arrest. Also reported were permanent neurological sequelae including aphasia, hemianesthesias, as well as motor impairments in the limbs. The reported effects of chronic use were paranoia, persecutory hallucinations, formications, loss of libido, anorexia, and insomnia, as well as "reckless abandon to the pursuit of the drug."

Based on the 1985 National Survey of Drug Abuse, 22 million Americans have tried cocaine and 12 million used the drug during the preceding year.

The accrued experience of untoward effects from cocaine led to a decline in its use by physicians and by the general public. Gradually, as narcotic drugs became criminalized, cocaine use faded into the background. Its use in medical practice remained restricted to local anesthesia, usually in ophthalmologic or otolaryngologic procedures.

The current wave of use probably had its origins in the 1950s, with accelerating numbers of cocaine users. Based on the 1985 National Survey of Drug Abuse, 22 million Americans have tried cocaine and 12 million used the drug during the preceding year. The most recent National Household Survey estimated that 8 million people had used cocaine in the

United States over the previous 12 months.⁵ However, the number of current users of cocaine appears to have declined — from 5.8 million users in 1985 to 2.9 million users in 1988.⁵

With increased use came increased morbidity. The Haight-Ashbury medical clinic reported a rise in cocaine use from less than 1 percent of patients seeking medical treatment in 1970 to greater than 6 percent in 1982.⁶ Reports from metropolitan emergency rooms show that in 1988 5.1 deaths per thousand involved cocaine (3,100 deaths nationwide). By contrast, in 11.1 deaths per thousand, heroin or morphine was mentioned. The number of emergency room reports of cocaine events was 13,501 compared to 21,090 for alcohol and 14,696 for heroin/morphine.

Cocaine Physiology and Pharmacology

Cocaine has four major physiological effects:

- 1) It is a highly potent local anesthetic, the only naturally occurring local anesthetic. It blocks the initiation and propagation of nerve impulses by affecting the sodium conductance of nerve cell membranes.

- 2) Cocaine is a potent sympathomimetic agent which potentiates the actions of catecholamines in the autonomic nervous system, producing tachycardia, vasoconstriction and hypertension.

- 3) Cocaine is a potent stimulant of the central nervous system, potentiating the action of central catecholamine neurotransmitters, norepinephrine and dopamine. Cocaine blocks the reuptake of these neurotransmitters into neurons, and may also cause neurotransmitter release. Its behavioral effects include increased arousal, euphoria, excitement and motor activation. At

high doses, this may progress to agitation, irritability, apprehension and paranoia.

- 4) Cocaine is perhaps the most powerful reinforcer known. Animals and humans given the opportunity to self-administer drugs will work harder to self-administer cocaine than any other drug.

Cocaine intoxication is characterized by elation, euphoria, excitement, pressured speech, restlessness, stereotyped movements and bruxism. Physiological signs of sympathetic stimulation are present, including tachycardia, mydriasis, and sweating. With chronic use, paranoia, suspicion and psychotic symptoms may occur. Overdose of cocaine produces hyperpyrexia, hyperreflexia and seizures, which can progress to coma and respiratory arrest.

Concentrations of cocaine in plasma depend on the dose administered and the manner in which the drug is taken. Although cocaine is initially rapidly absorbed from mucous membranes, such as oral or nasal mucosa, the potent vasoconstriction produced by the drug rapidly reduces the absorption of the drug from these sites and limits the amount of cocaine absorbed. In contrast, intravenous administration of freebase cocaine or smoking cocaine vapor does not retard absorption. The result is plasma levels of the drug many times higher than levels achieved through mucous membrane absorption.

The plasma half-life of cocaine following oral, nasal or intravenous administration is approximately 1 to 2 hours, which correlates with its behavioral effects.⁷ Cocaine has a biphasic plasma concentration-time curve, with a rapid peak, rapid decline due to redistribution, and a slower decline due to metabolism of the drug. Cocaine is metabolized to

inactive compounds by several plasma and tissue esterases including plasma pseudocholinesterase. With the decline in plasma levels, most users experience a period of dysphoria or "crash," which often leads to increased cocaine use over shorter periods. The dysphoria of this "crash" is intensified and prolonged following repeated use.

Identification and Diagnosis of Cocaine Users

While some patients may present with cocaine use or its sequelae as a chief complaint, many patients present with other medical or surgical problems and later reveal a substance-use disorder through physical or laboratory findings, or as an incidental discovery.

Cocaine is perhaps the most powerful reinforcer known.

For many reasons, patients who use psychoactive substances such as cocaine are usually reluctant to report their actual drug use to physicians or other health care providers. Patients and their family members often go to great lengths to deny the extent of substance-abuse problems. When cocaine use is suspected but a patient is unable or unwilling to give a history of cocaine use, it is important to obtain additional history from the patient's family or acquaintances. It is also helpful to examine other medications and drug paraphernalia in the patient's possession.

When taking information about the patient's alcohol and drug use, most clinicians routinely ask quantity and frequency questions about psychoactive substances, such as "how much?" and "how often?" Unfortunately, experience shows these questions to be relatively unreliable in accurately detecting substance abuse. A

more effective interview method focuses on whether the patient has experienced negative consequences from use of cocaine, has poor control of use, or has received criticism from others about his substance use.

Patients and their family members often go to great lengths to deny the extent of substance-abuse problems.

Abnormal results on laboratory testing provide an important adjunct to confirm the substance abuse diagnosis, but are not highly reliable or specific. No specific abnormal laboratory tests are highly associated with cocaine use. Serum and urine toxicological screens also may be unreliable and are affected by many factors, including sample collection and accuracy of laboratory methods. Unless testing closely follows active drug use, the short half-life of cocaine often makes detection difficult.

Medical Consequences of Cocaine Use

Medical consequences of cocaine use fall into two general categories, 1) those linked to method and route of drug administration and 2) those linked to pharmacological effects after the drug reaches body fluids.

Cocaine may be administered by several routes, each of which has associated morbidity. Intranasal insufflation of cocaine often results in rhinitis and recurrent nosebleeds and chronic use can lead to anosmia, nasal mucosal atrophy and nasal septal perforation.^{8, 9} Bilateral optic neuropathy and osteolytic sinusitis have been reported¹⁰ as well as midline ulceration of the respiratory tract.¹¹

Intravenous injection of co-

caine is associated with considerable morbidity. Many users experience tissue necrosis and infection at injection sites due to intense vasoconstriction from the drug, particularly when it extravasates into tissue. Inadvertent or planned arterial injection of cocaine can result in severe vasospasm and massive tissue injury.¹² Sharing needles and other injection paraphernalia exposed IV cocaine users to risks of contracting HIV, hepatitis B or other blood-borne infections.

Smoking and inhaling heated "crack" and freebase cocaine is associated with sore throat, dry chapped lips, black sputum, and hemoptysis.¹³ A decrease in diffusion capacity of alveolar membranes has been reported in cocaine smokers with normal-appearing chest radiographs¹⁴ and pulmonary hemorrhage has been reported.¹⁵ Propane torches and lighters used to volatilize cocaine have been implicated in pneumomediastinum and pneumopericardium.^{16, 17}

Oral ingestion of large amounts of cocaine occurs infrequently, but can result in intestinal ischemia leading to bowel perforation.¹⁸ Condoms or balloons filled with cocaine are sometimes ingested to smuggle drugs through customs or into prisons. Leakage or rupture of these containers can cause severe cocaine overdose.

The second category of medical consequences includes effects of cocaine which occur after the drug is distributed in body fluids. A major risk factor for cocaine-related morbidity and mortality appears to be impaired elimination secondary to an inherited deficiency of plasma pseudocholinesterase, which assists in the breakdown of the drug.¹⁴

Cardiovascular complications of cocaine use include acute myocardial infarctions, which can

occur even in coronary arteries documented as completely normal by angiography.^{19, 20} Myocarditis may result from chronic cocaine use,²¹ and has been documented in autopsy studies where 8 of 40 patients (20%) who had detectable cocaine or metabolites in bodily fluids showed evidence of myocarditis — as compared to 1 in 27 (3.7%) patients who were negative on toxicology screen.²² Cocaine-associated cardiac arrhythmias include sinus tachycardia, which almost always occurs with use of the drug; ventricular tachycardia and fibrillation; ventricular premature contractions, and asystole.²³ Systolic hypertension usually occurs with cocaine use and tolerance to this effect does not develop.²⁴ Severe hypertension can result in acute vascular damage, and rupture of the ascending aorta has been reported in a heavy cocaine smoker.²⁵

Neurologic disease may be a relatively common sequelae of cocaine use. A recent series describes 14 patients with a variety of neurologic syndromes temporally associated with cocaine use. These syndromes included relatively rare symptom-complexes resulting from anterior spinal artery syndrome, lateral medullary syndrome, transient ischemic attacks in the middle cerebral artery and vertebrobasilar artery territories as well as partial motor seizures.²⁶ Strokes may be due to hemorrhage or infarction, as is the case with three reported rostral midbrain strokes temporally related to cocaine use.²⁷ Subarachnoid hemorrhage can occur within minutes of intranasal cocaine use.²⁸

Cocaine use is a risk factor for seizures²⁹ which may appear in focal or generalized form. Convulsions also may appear as a terminal event secondary to cerebral hyperperfusion in cocaine-

associated deaths.³⁰ Migraine-like headaches following recreational cocaine use reportedly remit as the patient stops using the drug. Hyperthermia may be precipitated by acute cocaine exposure, and this may be associated with convulsions, as well. Neurological problems have occurred in children passively exposed to cocaine smoke. These included drowsiness and an unsteady gait in two children, as well as generalized seizures in two others.³¹ Dystonia can be seen in the setting of cocaine withdrawal, as well as with acute cocaine exposure.^{32, 33} Chronic cocaine use is associated epidemiologically with the development of panic attacks.³⁴

Neurological problems have occurred in children passively exposed to cocaine smoke.

Reports of gastrointestinal toxicity include gastropyloric ulcers associated with use of "crack,"³⁵ as well as possible hepatotoxicity associated with cocaine use.³⁶

Obstetrical complications of cocaine use vary; they result from direct teratogenic effects of the drug as well as indirect toxic effects on the uterine environment. Urogenital malformations occur with a much higher frequency in the offspring of cocaine-using mothers, even when controlled for other drug use.³⁷ Cocaine use during pregnancy results in a higher rate of microcephaly and intrauterine growth retardation.³⁸ Sudden infant death syndrome is more common in neonates exposed to cocaine than in controls. Cocaine-exposed infants are also more likely to have cardiorespiratory pattern abnormalities associated with SIDS.³⁹ Follow-up neurological studies of children born to cocaine-using mothers are

warranted because of mounting evidence of long-term neurological impairment.⁴⁰ Abruptio placenta is a documented complication of maternal use.⁴¹ The rate of spontaneous abortion is higher in cocaine-using mothers.⁴²

Treatment

Treating cocaine users requires an ability to identify cocaine abuse or dependence, to manage intoxication and withdrawal therapies, and to understand options for long-term rehabilitation and treatment. In addition, clinicians must be aware of their own attitudes and biases toward substance abuse and patients. Negative attitudes toward substance abuse are common among physicians and interfere with appropriately identifying and treating substance-abuse patients.

While the optimal treatment of cocaine users is still not established, the physician should be aware of general principles applying generally to all substance abuse and dependence treatment. To establish an effective therapeutic relationship is the primary task of the physician. In this relationship, the physician needs to conduct a detailed alcohol and drug history, make an appropriate physical examination, order and interpret necessary laboratory tests, engage the patient and family in appropriate short-term or long-term substance abuse treatments and manage the acute and long-term consequences of the substance abuse.

During short-term treatment, goals include stopping cocaine use and achieving a drug-free state. The physician should determine the extent of cocaine use and the ability and desire of the patient to achieve abstinence. If initial efforts to abstain fail, a substance abuse specialist or specialized substance abuse program

should be considered. Although outpatient treatment should be considered initially, inpatient hospitalization often is necessary to achieve cocaine abstinence. Self-help programs, such as Narcotics Anonymous, and Cocaine Anonymous can be extremely helpful and supportive for some patients, and should be suggested for all cocaine users. Pharmacological treatment may hasten abstinence by decreasing craving and other withdrawal signs and symptoms.

In the long-term phase of treatment, the patient undergoes a process of rehabilitation and attempts to reestablish a viable, drug-free lifestyle. Rehabilitation should be tailored to the individual and may consist of outpatient treatment and monitoring, inpatient treatment in an extended inpatient rehabilitation program (usually about 3-4 weeks), or a long-term residential treatment program (usually several months long).

Most patients presenting for treatment do so in the context of a family structure, which is also experiencing dysfunction. It is important for the clinician to be aware of dysfunctional family dynamics, and the denial, defensiveness and hostility often present in family members. Family members also need education, as well as emotional and social support. Organizations such as Narc Anon provide meaningful education and support for spouses and family members. It is important to involve family members in the patient's treatment as much as possible, as well as to recommend treatment for other family members, when appropriate.

While cocaine withdrawal is not as severe as with opioids or alcohol, many individuals who stop taking cocaine experience a variety of unpleasant signs and symptoms including dysphoria,

depression, nausea, vasomotor instability and severe drug craving. Patients frequently describe vivid dreams about cocaine. These effects are often intense and make abstinence harder.

Psychotherapy, group therapy and behavior modification have been found to be useful to maintain abstinence.⁴³ A variety of pharmacological agents have shown promise as adjunctive treatments. Several reports have shown efficacy of antidepressant agents such as imipramine, desipramine, lithium or trazodone in reducing cocaine craving and usage.^{44, 45, 46} The doses of medication used are similar to those used for antidepressant therapy. As it appears to block cocaine craving, the post-synaptic dopamine agonist bromocriptine also may have usefulness in cocaine treatment.⁴⁷

... clinicians must be aware of their own attitudes and biases toward substance abuse and patients.

Intoxication with other sympathomimetic agents such as amphetamines, methylphenidate, and other stimulants may produce a similar clinical picture as cocaine intoxication, including sympathetic and behavioral hyperactivity. A potent form of methamphetamine, often called "crank," (or "ice") is now being sold along with crack and some cocaine on the street is actually crank instead of crack. An "amphetamine psychosis," with manifestations of agitation, paranoia, delusions and hallucinosis, may follow chronic use of this drug. Antipsychotic medication such as haloperidol is useful in the treatment of stimulant psychoses; however, such patients may frequently require psychiatric hos-

pitalization. Severe hypertension is seen in overdose, and may be treated with alpha-adrenergic blockade.

Conclusion

The prevalence of cocaine use and the medical, psychiatric and social consequences of such use are considerable. Even sporadic or recreational use of cocaine may have immediate deleterious effects on health. All physicians should be familiar with the health effects of cocaine and should be able to recognize cocaine use in their patients. In addition, physicians should be aware of treatment options and treatment resources for their cocaine-using patients.

References

- 1 Siegel RK, "Intoxication, Life in Pursuit of Artificial Paradise" E.P. Dutton New York 1989.
- 2 Becker HK, Carl Koller and Cocaine. *Psychoanalytic Quarterly*. 32:309, 1963.
- 3 Penfield W. Halsted of Johns Hopkins. *JAMA* 210:2214-2218, 1969.
- 4 Norris GW. A case of cocaine habit of three months duration, treated by complete and immediate withdrawal of the drug. *Philadelphia Medical Journal* 1:304, 1901.
- 5 Holden C. Cocaine Trends. *Science* 245:1192, 1989.
- 6 Gay GR. Clinical management of acute and chronic cocaine poisoning. *Ann Emergency Medicine* 11:562-572, 1982.
- 7 Van Dyke C, Jatlow P, Ungerer J, et al: Oral cocaine: plasma concentration and central effects. *Science* 200:211-213, 1978.
- 8 Vilenky W. Illicit and licit drugs causing perforation of the nasal septum. *J Forensic Sci*. 27:958-962, 1982.
- 9 Schwartz RH, Estroff T, Fairbanks DN, Hoffmann NG. Nasal symptoms associated with cocaine abuse during adolescence. *Arch Otolaryngol Head Neck Surg* 1989 Jan;115(1):63-4.
- 10 Newman NM, DiLoreto DA, Ho JT, Klein JC, Birnbaum NS. Bilateral optic neuropathy and osteolytic sinusitis. Complications of cocaine abuse. *JAMA* 1988 Jan 1;259(1):72-4.
- 11 Becker GD, Hill S. Midline granuloma due to illicit cocaine use. *Arch Otolaryngol Head Neck Surg* 1988 Jan;114(1):90-1.
- 12 Berger JL, Nimier M, Desmonts JM. Continuous axillary plexus block in the treatment of accidental intraarterial injection of cocaine [letter]. *N Engl J Med* 1988 Apr 7;318(14):930.
- 13 Siegal RK. Cocaine free base use. *J Psychoactive Drugs*. 14(4):311-319, 1982.
- 14 Itkonen J, Schnoll S, Glassroth J. Pulmonary dysfunction in "freebase" users. *Arch Intern Med*. 144:2195-7, 1984.

- ¹⁵ Walek JW, Masson RG, Siddiqui M. Pulmonary hemorrhage in a cocaine abuser [letter]. *Chest* 1989 Jul;96(1):222.
- ¹⁶ Morris JB, Shcuk JM. Pneumomediastinum in a young male cocaine user. *Ann Emerg Med*. 14:194-196, 1985.
- ¹⁷ Androuny A, Magnusson P. Pneumopercardium from cocaine inhalation. *N Eng J Med*. 313:48-49, 1985.
- ¹⁸ Nalbandian H, Sheth N, Dietrich R, Georgiou J. Intestinal ischemia caused by cocaine ingestion, report of two cases. *Surgery*. 132:495-500, 1978.
- ¹⁹ Isner JM, Estes NAM III, Thompson PD. Acute cardiac events temporally related to cocaine use. *N Eng J Med*, 315:1438-1443, 1986.
- ²⁰ Fernandez MS, Pichard AD, Marchant E, Lindsay J Jr. Acute myocardial infarction with normal coronary arteries: in vivo demonstration of coronary thrombosis during the acute episode. *Clin Cardiol* 6:553-9, 1983.
- ²¹ Jentzen JM. Cocaine-induced myocarditis [letter]. *Am Heart J* 1989 Jun;117(6):1398-9.
- ²² Virmani R, Robinowitz M, Smialek JE, Smyth DF. Cardiovascular effects of cocaine: an autopsy study of 40 patients. *Am Heart J* 1988 May;155(5):1068-76.
- ²³ Nanji AA, Filipenko JD. Asystole and ventricular fibrillation associated with cocaine intoxication. *Chest* 85:132-3, 1985.
- ²⁴ Foltin RW, Fischman MW, Pedrosos JJ, Pearson GD. Repeated intranasal cocaine administration: lack of tolerance to depressor effects. *Drug Alcohol Depend* 1988 Dec;22(3):169-77.
- ²⁵ Barth CW III, Bray M, Roberts WC. Rupture of the ascending aorta during cocaine intoxication. *Am J Cardiol*. 57:496, 1986.
- ²⁶ Mody CK, Miller BL, McIntyre HB, Cobb SK, Goldberg MA. Neurologic complications of cocaine abuse. *Neurology* 1988 Aug;38(8):1189-93.
- ²⁷ Rowley HA, Lowenstein DH, Rowbotham MC, Simon RP. Thalamomesencephalic strokes after cocaine abuse. *Neurology* 1989 Mar;39(3):428-30.
- ²⁸ Schwartz KA, Cohen JA. Subarachnoid hemorrhage precipitated by cocaine snorting. *Arch Neurol* 41:705, 1984.
- ²⁹ Choy-Kwong M, Lipton RB. Seizures in hospitalized cocaine users. *Neurology* 1989 Mar;39(3):425-7.
- ³⁰ Mittleman RE, Wetli CV. Death caused by recreational cocaine use: an update. *JAMA* 252:1889-93, 1984.
- ³¹ Bateman DA, Heagarty MC. Passive free-base cocaine ("crack") inhalation by infants and toddlers. *Am J Dis Child* 1989 Jan;143(1):25-7.
- ³² Choy-Kwong M, Lipton RB. Dystonia related to cocaine withdrawal: a case report and pathogenic hypothesis. *Neurology* 1989 Jul;39(7):996-7.
- ³³ Merab J. Acute dystonic reaction to cocaine [letter]. *Am J Med* 1988 Mar;84(3 Pt 1):564.
- ³⁴ Anthony JC, Tien AY, Petronis KR. Epidemiologic evidence on cocaine use and panic attacks. *Am J Epidemiol* 1989 Mar;129(3):543-9.
- ³⁵ Abramson DL, Kral JG, Gertler JP, Lewis T. Gastropyloric ulcers related to "crack" [letter]. *JAMA* 1989 Aug 4;262(5):617-8.
- ³⁶ Shuster L, Garhart CA, Powers J, Grunfeld Y, Kanel G. Hepatotoxicity of cocaine. *NIDA Res Monogr* 1988;88:250-75.
- ³⁷ Urogenital anomalies in the offspring of women using cocaine — during early pregnancy — Atlanta, 1968-1980. *MMWR* 1989 Aug 11;38(31):536, 541-2.
- ³⁸ Hadeed AJ, Siegel SR. Maternal cocaine use during pregnancy: effect on the newborn infant. *Pediatrics* 1989 Aug;84(2):205-10.
- ³⁹ Chasnoff IJ, Hunt CE, Kletter R, Kaplan D. Prenatal cocaine exposure is associated with respiratory pattern abnormalities. *Am J Dis Child* 1989 May;143(5):583-7.
- ⁴⁰ Dow-Edwards DL. Long-term neurochemical and neurobehavioral consequences of cocaine use during pregnancy. *Ann NY Acad Sci* 1989;562:280-9.
- ⁴¹ Acker D, Sachs BP, Tracey KJ, Wise WE. Abruptio placentae associated with cocaine use. *Am J Obstet Gyn*. 146:220-1, 1984.
- ⁴² Chasnoff IJ, Burns WJ, Schnoll SH, Burns KA. Cocaine use in pregnancy. *N Eng J Med*. 666-9, 1985.
- ⁴³ Rounsaville BJ, Gawin FH, Kleber HD: Interpersonal psychotherapy adapted for ambulatory cocaine users. *Am J Drug Alc Abuse* 11:171, 1985.
- ⁴⁴ Rosecan JS: The psychopharmacologic treatment of cocaine addiction (abstract), VII World Congress of Psychiatry, Vienna, 1983.
- ⁴⁵ Tennant FS, Rawson RA: Cocaine and amphetamine dependence treated with desipramine, in: Harris L(ed) Problems of Drug Dependence. NIDA Monograph Series 43. National Institute of Drug Abuse, Rockville, MD, 351-355, 1983.
- ⁴⁶ Gawin F, Kleber H: Pharmacologic treatments of cocaine abuse. *Psychiatric Clin North America* 9(3):573-583, 1986.
- ⁴⁷ Dackis CA, Gold M: Bromocriptine as treatment of cocaine abuse. *Lancet* 1:1151, 1985.

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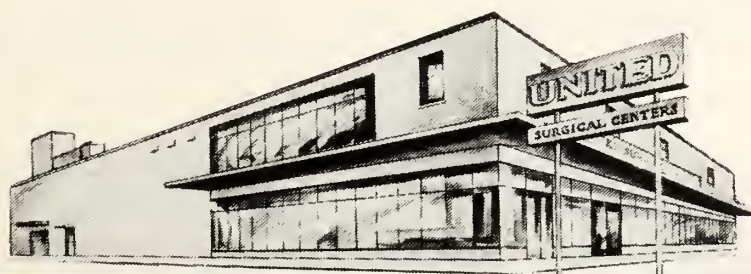
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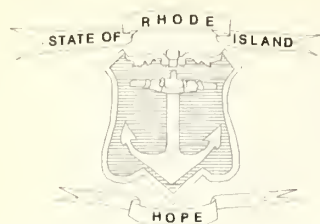
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Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

Statewide Prevalence of Cocaine Use During the Perinatal Period

The use of cocaine during pregnancy is a growing public health problem. Due to a reported increase in its use and a concern over the severe negative effects on pregnant women and their newborns, the Rhode Island Department of Health conducted a statewide prevalence study of perinatal drug use. The purpose of this study was to determine the need for services for pregnant women and to provide baseline data to see how the drug problem changes over time.

During a seventeen day period in October/November 1989 all eight maternity hospitals in the state provided the Department of Health with aliquots of urine specimens collected from all pregnant women admitted in active labor. The urine specimens were tested for cocaine, opiates, marijuana, and amphetamines. Only the cocaine results will be reported here. (See CDC, MMWR, Vol. 39:14, April 13, 1990 for full results of the study.)

Each urine specimen was tested by enzyme-multiplied immunoassays for cocaine metabolites. Toxicology screen cutoffs for cocaine were 300 ng/ml. Cocaine is likely to be detected in the urine for 1-2 days after use.

There were 465 samples collected, represented in 65.2% of all births occurring during the seventeen days of the study. An analysis of all births in the period demonstrated the representativeness of the sample.

Thirty-five of the 465 urine specimens tested positive for at least one drug, representing a statewide prevalence rate of 7.5%. Cocaine users comprised 2.6% of this 7.5% sample (Figure 1). This percentage was used to estimate the minimum number of perinatal cocaine users in need of counseling and treatment each year: 364.

Cocaine users had the most distinct sociodemographic profile of any of the drug users. As Table 1 shows, cocaine use was significantly higher in women who were on public insurance (8.9% compared to 0.3%); non-white (8.1% compared with 1.1%); living in "poverty"

census tracts (6.8% compared to 0.9%); giving birth to a second or higher birth order child (4.2% compared to 0.5%) and delivering at Women and Infants Hospital (3.9% compared to 1.0%). Figure 2 shows a risk profile of the perinatal cocaine users found in our study.

Rates of perinatal cocaine abuse reported in the literature range from 9% to 14%. These studies were not population based, but selected high risk populations from inner city hospitals for screening. The Rhode Island study is unique because it includes all births at both inner city and community hospitals. Although the Rhode Island rate is lower, it is a better measure of the extent of perinatal cocaine abuse in a statewide maternity sample.

Table 1: Characteristics of the Pregnant Women Who Use Cocaine During the Perinatal Period

SOCIO-DEMOGRAPHIC CHARACTERISTIC

SOCIO-DEMOGRAPHIC CHARACTERISTIC	TOTAL NUMBER SCREENED	USED COCAINE %	(N)
RACE			
White	356	1.1**	(4)
Non-white	98	8.1	(8)
PARITY			
1st Birth	194	0.5*	(1)
> = 2nd Birth	260	4.2	(11)
AGE			
< 25	154	3.2	(5)
> = 25	300	2.3	(7)
INSURANCE			
Private	316	0.3**	(1)
Public	124	8.9	(11)
GEOGRAPHIC			
Poverty Census Tracts	118	6.8**	(8)
All Other	334	0.9	(3)
HOSPITAL			
WIH	259	3.9*	(10)
Others	199	1.0	(2)
TOTAL	465	2.6	(12)

* p-value < 0.01

** p-value < 0.001

Source: Perinatal Drug Survey, Division of Family Health

Figure 1: Perinatal Drug Use in Rhode Island

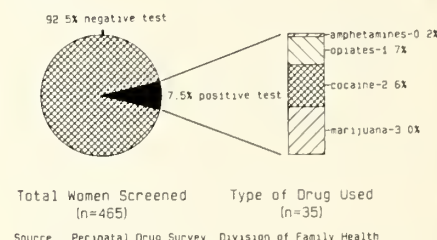
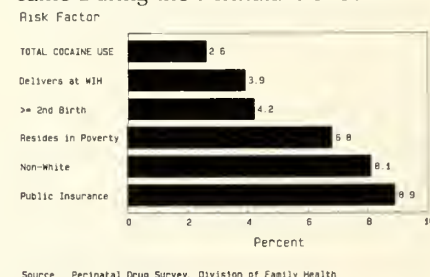


Figure 2: Who is at Risk for Abusing Cocaine During the Perinatal Period?



Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with February 1990	
	February 1990 Number	Number	Rates
Live Births	1,176	15,405	15.5*
Deaths	782	9,770	9.8*
Infant deaths	(12)	(160)	10.4†
Neonatal deaths	(11)	(130)	8.4*
Marriages	377	8,302	8.4*
Divorces	350	3,707	3.7*
Induced Terminations	666	7,922	514.2†
Spontaneous Fetal Deaths	57	1,093	71.0†
Under 20 weeks' gestation	(49)	(976)	63.4†
20 + weeks' gestation	(8)	(106)	6.9†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with November 1989		
	November 1989 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	264	3,420	344.4	4,687.0
Malignant Neoplasms	194	2,451	246.8	6,986.5
Cerebrovascular Diseases	43	593	59.7	970.0
Injuries (Accident, Suicide, Homicide)	36	442	44.5	10,209.5
COPD	30	310	31.2	453.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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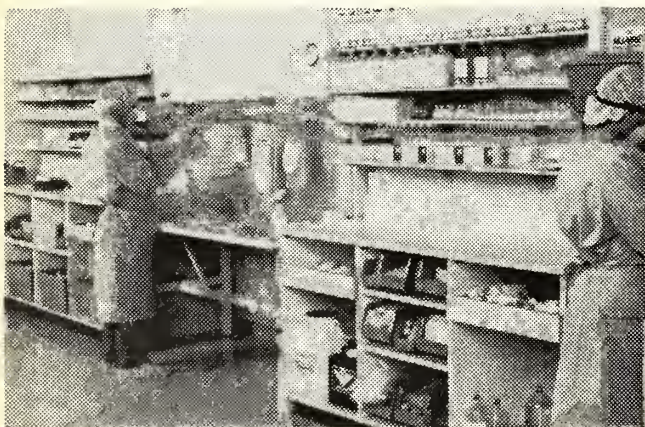
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Issued Monthly under the direction of the Publication Committee

VOLUME 1
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (June, 1940)

The lead article is entitled, *Gastroscopy and Clinical Medicine* and is authored by Dr Russell Bray of Angell Street, Providence. The article attempts "to portray by word pictures my impression of gastroscopy and to tell in general the value and limitations of the procedure. Visual inspection of the inside of the human stomach tends to quicken the emotions. The observer cannot help but respond to the beauty of the scene — the array of color, the rhythmic contractions of the pylorus, the bubbling pools of secretion, the dancing highlights, and the shifting shadows cast by the rugal folds!"

The author lists the following contraindications to gastroscopy: (1) Obstructing lesion at the cardio-esophageal orifice. (2) Positive disease of the chest — cardiac disease, aneurysm of the aorta, angina, dyspnea. (3) Varices of esophagus, a large liver. (4) Uncooperative patient. (5) Dysphagia. (6) Do not use the procedure when tired or hurried.

The author summarizes his experiences as follows: "(1) If gastroscopy is to remain a procedure of value, claims for its usefulness must be based on facts. An attitude of reasonable conservatism

will be most favorable to the continued progress of gastroscopy. (2) The Wolf-Schindler flexible gastroscope allows the observer to actually see what is going on in the stomach. (3) It is the one positive means of diagnosing gastritis. (4) Gastroscopy allows the differential diagnosis of benign and malignant ulcer. (5) Gastroscopy may reveal the origin of gross hematemesis. (6) It must be understood that the gastroscope will not, and cannot, supplant the X-ray in the diagnosis of gastric disease. An experienced roentgenologist, however, will not hesitate to admit that he frequently encounters mucosal patterns and profile distortions which are of doubtful diagnostic value. Therefore, gastroscopy is always of value in checking X-ray findings. X-ray and gastroscopy are complementary rather than competitive methods of diagnosis."

The second major paper, by Drs Charles A. McDonald and Milton Korb, is entitled, "Brain Abscess with Brain Potentials." The paper describes the 1937 case of a 17-year-old male admitted to the neurological service of the Rhode Island Hospital because of blurred vision, headaches, some projec-

tile vomiting and dizziness. There was also an older history of head injury. Because of choked discs, elevated spinal fluid pressure and a number of focal and general neurologic deficits, a diagnosis of "brain tumor of the left cerebral hemisphere was made." Electroencephalographic examination pointed to a pathologic condition in the left frontal lobe. *(These EEGs were interpreted by Dr H. Jasper who later transferred to the Montreal Neurological Institute to become, with his colleague Wilder Penfield, one of the world's leading authorities on electroencephalography.)* The patient was transferred to a Boston hospital where ventriculography was performed and the X-rays were consistent with a mass deep within the left frontal lobe. Three days later a craniotomy was undertaken and a suppurative brain abscess was resected. The patient died a few days later of meningitis.

An autopsy disclosed a linear fracture of the ethmoid bone involving the frontal sinus and was considered the likely mechanism causing the intracerebral abscess. This case is notable in being "one of the first cases in which electroencephalographic

examination was used as a clinical laboratory test."

The *Journal* also publishes the proceedings of a symposium on post-operative distension, with contributions by Drs William P. Davis, Eliot A. Shaw, and Henry B. Moor. In summary, "the care of the patient suffering with distension is along two major lines. First, care of the distension itself, and second, care of the disturbed physiology associated with distension. In the care of the former — the following methods have been considered: the use of the intestinal stimulants, physostigmine, prostigmin, pituitrin, and peristaltine. The value of morphine as an intestinal stimulant has been mentioned. The use of 95% oxygen, and intestinal drainage by the Wangensteen and the Miller-Abbott tubes have been considered. In furthering the idea of intestinal drainage, ileostomy has been discussed and three case studies presented. The patient's bodily requirements as dextrose, water, and chlorides have been reviewed. The indication for transfusion has been presented."

An editorial discusses President F.D. Roosevelt's proclamation designating April as Cancer Control Month, and the educational work undertaken by the American Cancer Society, an organization formed in 1913. Yet another editorial expresses support for pending legislation in Congress (Wagner-George bill) which provides federal funds for the construction of civilian hospitals.

Another editorial reflects upon the State Infirmary at Howard "... dispensing alms to hapless people who had no homes, no future, no folks to shelter their declining years. The stigma of spending one's last days at Howard in the State Infirmary was a real dread to many an oldtimer in

Rhode Island. All this has been changed."

The official program for the 129th annual meeting of the Rhode Island Medical Society is published, listing the many participating hospitals including the Homeopathic Hospital of Rhode Island (now, Roger Williams General Hospital), the Providence Lying-In Hospital (now, Women & Infants Hospital), Butler Hospital and Memorial Hospital of Pawtucket.

Twenty-Five Years Ago (June, 1965)

A book review by Dr Robert V. Lewis comments on "Doctors as Men of Letters" noting that "The study of medicine played some part in the development of these writers," listing such personages as Browne, Locke, Smollett, Goldsmith, E. Darwin, Shelley, Keats, C. Darwin, O.W. Holmes, Blackwell, T.H. Huxley, Conan Doyle, Grenfell, G. Stein, Somerset Maugham, Z. Grey, Joyce, and Jeffers. The reviewer ends his commentary with these words, "... but as in all things, it is only when technique is imbued with a humane spirit that any work of man becomes great. The contemplations and contributions of doctors as men of letters are good to behold."

The lead article is entitled, "Regional Hypothermia II — Effectiveness of Renal Artery and Renal Pelvic Perfusion Methods." and is written by Drs S.H. Yoon and E.K. Landsteiner. The authors conclude that the optimal cooling time in renal artery perfusion, in the dog, is about 5 minutes, and that it represents a fast and simple method for achieving renal hypothermia, but that the risk of thrombus formation must be considered.

The presidential address by Dr John C. Ham stresses the fundamental importance of health ed-

ucation in providing better health for Rhode Islanders. Dr Ham also urges that a Health Museum for Rhode Island be established and funded.

By use of histochemical techniques, Drs B. Barker and P. Farnes, demonstrate the vascular networks within aspirated human bone marrow particles. An unusual distortion of this vascular architecture is described in two cases of multiple myeloma.

Dr W. Fischer writes about survival time in Hodgkin's Disease, based upon experience at Rhode Island Hospital, 1946 to 1962. He notes that paraganuloma and granuloma survivals are equal and twice that of the sarcoma type. And despite some cautious correlations, the author concludes, "It is dangerous to predict treatment response or survival in any given case of Hodgkin's Disease."

In honoring the University of Pennsylvania on its bicentennial anniversary, an editorial comments: "We salute the University of Pennsylvania on its most successful career and upon the completion of the first two hundred years of medical education in America. We also pay tribute to those dedicated trustees in the state of Rhode Island who in the Franklin tradition have given their time and effort to the development of the finest of hospital facilities. We expect the outstanding feature of Brown's third century to be its Medical School."

Without editorial comment, the *Journal* prints an observation by William Osler: "No man is really happy or safe without a hobby, and it makes precious little difference what the outside interest may be — botany, beetles or butterflies; roses, tulips or irises; fishing, mountaineering or antiques — anything will do so long as he straddles a hobby and rides it hard."



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Hypotension: Excessive hypotension is rare in uncomplicated hypertensive patients treated with VASOTEC alone. Patients with heart failure given VASOTEC commonly have some reduction in blood pressure, especially with the first dose, but discontinuation of therapy for continuing symptomatic hypotension usually is not necessary when dosing instructions are followed, caution should be observed when initiating therapy. (See DOSAGE AND ADMINISTRATION.) Patients at risk for excessive hypotension, sometimes associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death, include those with the following conditions or characteristics: heart failure, hypotension, high-dose diuretic therapy, recent intensive diuresis or increase in diuretic dose, renal dialysis, or severe volume and/or salt depletion of any etiology. It may be advisable to eliminate the diuretic (except in patients with heart failure), reduce the diuretic dose, or increase salt intake cautiously before initiating therapy with VASOTEC in patients at risk for excessive hypotension who are able to tolerate such adjustments. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients at risk for excessive hypotension, therapy should be started under very close medical supervision and such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart disease or cardiovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of VASOTEC, which usually can be given without difficulty once the blood pressure has stabilized. If symptomatic hypotension develops, a dose reduction or discontinuation of VASOTEC or concomitant diuretic may be necessary.

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: General Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The likelihood of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta-adrenergic-blocking agents, methyldopa, nifedipine, calcium-channel blocking agents, hydralazine, prazosin, and digoxin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radiocactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not

been clearly defined, VASOTEC® (Enalapril Maleate, MSO) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome: Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably resulting from decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypotension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of 14 C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2987 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), angina pectoris (1.5%), nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring during the trial was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients (see WARNINGS, Hypotension), pulmonary embolism and infarction, pulmonary edema, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis (hepatocellular or cholestatic jaundice), melena, anorexia, dyspepsia, constipation, glossitis, stomatitis, dry mouth.

Musculoskeletal: Muscle cramps.

Nervous/Psychiatric: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Respiratory: Bronchospasm, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, anosmia, tinnitus, conjunctivitis, dry eyes, hearing.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgia, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 11% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol %, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: Hypertension: In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed.

If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium (see PRECAUTIONS).

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance >30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 2.5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure who have hyponatremia (serum sodium <130 mEq/L) or with serum creatinine >1.6 mg/dL, therapy should be initiated at 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d. then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more. If at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function, the maximum daily dose is 40 mg.

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AIDS
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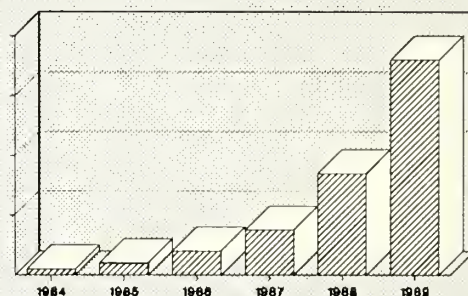


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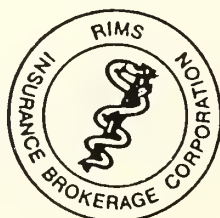
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EDITORIALS

AIDS and Physicians in Rhode Island: Resources and Responsibilities

By the close of the recent decade, there have been more than 300 persons diagnosed with AIDS in Rhode Island, with 150 succumbing to this disease. The best estimates by the Rhode Island Health Department suggest that there are several thousand individuals infected with HIV, the virus that causes AIDS. Data from cohorts that have been followed for many years suggest that the rate of the development of opportunistic infections and neoplasms in HIV-infected persons increases with time.

Over the next few years we face the specter of an increase in the rate of the development of new cases of AIDS whether or not Rhode Islanders decrease their risks for HIV transmission. The article by Dr Sally Zierler and colleagues summarizing the New England Behavioral Health Study, an NIH-funded evaluation of the incursion of HIV among heterosexually active adults in Rhode Island, suggests continued cause for concern since the majority of self-identified high-risk individuals have indicated that they are not routinely using condoms or taking other protective measures. On the other hand, the findings of several recent AZT treatment studies suggest that there is some basis for optimism. With a mean follow-up of one year (a relatively short period of time given the chronic nature of HIV infection), a national network of investigators has been able to show that the use of AZT in persons who

have decreased T helper lymphocyte counts (< 500 cells/mm³) but have few or no symptoms of HIV infection, can delay the onset of HIV-related morbidity and mortality. We do not yet know whether drug toxicity or HIV resistance will obviate this benefit after longer term AZT usage.

Therefore the 1990s open with this paradox: the promise of early intervention, and the threat of the continued spread of the virus. There is much to be done by public health officials, academic investigators, but most importantly, by the clinical care community. As pointed out by Dr Alvan Fisher, AIDS is an illness that belongs in the purview of the primary care practitioner despite the fact that the management of specific opportunistic infections and neoplasms that arise in HIV immunocompromised hosts may require the assistance of subspecialty consultation. The initial work-up of the person at risk for HIV infection requires careful assessment and counseling, particularly with regard to issues around sexuality and drug usage. A number of specialized tests are used, but given the chronic nature of HIV infection and the complex psychosocial and medical needs posed by patients at risk for HIV infection, it is extremely important for primary care physicians to be the key providers of care for these individuals. HIV-infected persons may need to see infectious disease specialists, hematologist/oncologists, psychia-

trists, neurologists, dermatologists, and internal medicine subspecialists, and thus clearly need a well-trained primary care physician to integrate their care. Moreover, at the present time, seroprevalence studies suggest that the majority of individuals *at risk* for HIV infection are still not infected with the virus, so there is an important role for preventive education which attempts to modify risk-related behaviors.

What resources are available to the primary care physician to manage individuals at risk for HIV infection? First of all, the Department of Health maintains an anonymous testing program that can provide free HIV testing and counseling and may be contacted by any resident of the state by calling 277-2362. The State Health Department has also maintained an active program of training HIV counselors and clinicians in the clinical care community through a three day CDC approved HIV counseling course and a series of educational forums targeted to providers. In conjunction with the Brown University AIDS Program, and through a grant from the New

ABBREVIATIONS USED:

AIDS: *Acquired Immune Deficiency Syndrome*

AZT: *Azidothymidine (present name, Zidovudine)*

CDC: *Centers for Disease Control*

HIV: *Human Immunodeficiency Virus*

England AIDS Education and Training Center, clinicians have been offered a wider array of AIDS education and training opportunities. Members of the Brown University AIDS Program have participated in a series of Grand Rounds at hospitals in Rhode Island, small group didactic sessions, clinical practica, as well as day-long courses for clinicians to update their data bases and clinical skills. Several of the Brown University-affiliated teaching hospitals, particularly the Rhode Island Hospital, Miriam Hospital, and Memorial Hospital, maintain ongoing AIDS/HIV clinics and are able to accept referrals of patients with complex HIV management issues, and have also participated in the training of community-based, AIDS/HIV knowledgeable primary providers. The Health Department has sent out a variety of educational materials including the 180 page resource manual and clinical management review entitled "AIDS Guide" for all licensed physicians in Rhode Island. The guide is available through the Rhode Island Department of Health's AIDS Program and can be obtained by calling 277-2362. Further questions regarding upcoming opportunities in AIDS-specific training can be answered by calling the Brown University AIDS Program at Memorial Hospital at 722-6000, ext. 2602, or the AIDS Education office at the Rhode Island Health Department at 277-2362. The Health Department may be contacted to refer potential clients for HIV antibody screening through the anonymous testing program. Another option is the New England Behavioral Health Study which can provide free, confidential HIV screening for individuals who are heterosexually active and older than 18 years of age (telephone number: 725-3030).

The key message of this editorial is that the HIV epidemic is not going to go away very soon, but the medical system is doing a better job at transforming it into a manageable, chronic disease process. A system now exists in Rhode Island which can assist in the identification of individuals at risk for HIV infection, provide counseling and resources for those who are not yet infected but whose behavior places them at increased risk, and provide the appropriate services for those individuals who are infected. The key part of this system is the primary care provider community. We need feedback to know how we can best make the system optimally serve the needs of providers and patients.

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 State Epidemiologist
 Medical Director
 Office of Disease Control
 Rhode Island Department of Health

AIDS INFORMATION — WHOM TO CALL

General Information:

RI PROJECT AIDS:

Administrative Office	831-5522
Hotline (English/Spanish)	726-3010
In Newport	847-7229

MIRIAM HOSPITAL:

AIDS Information Hotline	331-8500, ext: 4025
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AIDS Testing Screening:

RI Department of Health	277-2362
RI Hospital AIDS Clinic	277-4741
RI Medical Society	331-3207
RI Blood Center	863-8393
RI Group Health Assoc., Providence (Subscribers call their own center)	331-3000
New England Behavioral Health Study	725-3030
Hemophilia Center of RI	277-8250

IN MASSACHUSETTS:

Massachusetts Department of Health: Hotline	617-522-4090
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From Whence Cometh This Dread Pestilence?

Disease, particularly communicable disease, represents an important deterrent in the progress of people and their nations. And when communicable disease strikes, it delivers not one but two burdens: first, the weight of the sickness itself; and second, the social perception, often the stigma, of that sickness. On the one hand, it diminishes our state of health; and on the other hand, it contrives to insert our illness, and often ourselves, into a tapestry of moral values.

Some communicable diseases carry a negligible stigma, typically those which are airborne, viral infections such as small-pox, influenza and measles. This is largely so because they are so widespread that socioeconomic factors do not play an obvious role in determining their selective attack rate.

On the other hand, when a communicable disease is restrictive in its attack rate, it may then be perceived as something other than a randomly distributed happenstance. And if this disease consistently selects a disadvantaged segment of the population, we then may impart to the disease those social qualities which characterize the affected population. The disease becomes more than an unfortunate interaction between host and pathogen: it becomes a metaphor and a vehicle for expressing judgmental disapproval of one or another way of life. When this happens, the rules of clinical epidemiology give way to the imperatives of moral judgment. When we think, in the abstract, of a patient with influenza, an essentially neutral picture comes to mind; when, however, we think of a patient with typhus,

or gonorrhea, or leprosy or AIDS, the imagery is likely to be notably different.

Clearly, when we assign value judgments to disease, we end up with a list of illnesses ranked by their degree of social acceptability. We then avoid some for reasons other than their morbidity and mortality. The "closet" diseases have changed from time to time as our social values have altered. Thus, tuberculosis and cancer were until recently, unmentionable diseases. When certain presidents of the United States died of neoplastic disease, a variety of euphemisms were employed in the news reports and rarely — until recently — did any obituary, presidential or otherwise, ever mention the "C" word.

But the closet harboring unmentionable diseases is not yet empty. There still lingers AIDS, a tragedy of immense worldwide proportions and one which now requires the most from medical practitioners and medical research workers.

It is instructive to see how our community confronted yet another and hitherto unknown communicable disease some 158 years ago. At that time, 1832, when Providence was a thriving seaport of 27,000 persons in a nation governed by our seventh president, Andrew Jackson, an utterly new disease called Asiatic Cholera swept in from Europe. It progressed westward through Europe, eventually across the Atlantic, seeding itself first in the squalid ghettos of New York before spreading throughout the nation; it was anxiously watched and carefully reported. Its etiology was unknown, its pathophysiology a mystery and its capricious spread

making it seem unlikely that it was contagious. Little could be done but consider quarantines, days of fasting or communal prayers.

The local sermons rendered during this apocalyptic summer of 1832 provide us with some notion of how this new pestilence was perceived. The following excerpts, delivered by one of the great religious leaders of this community, are from a sermon entitled, "On the Moral Uses of the Pestilence." Its message is remarkably similar to many other sermons and newspaper editorials of that fateful summer in 1832.

From the plains of India, from the mountains of central Asia, its march has been steady and irresistible; it has traversed deserts and seas; it has broken through all the defenses which the power and vigilance of governments could set up against it; till that which, for years, has been the rumor of far off evils, is suddenly become terrific reality; and the despoiler of two continents knocks at the door of our American homes.

At such a visitation, it is meet that the world should pause. It is meet that days of fasting and humiliation and prayer should suspend the ordinary pursuits and cares of life, and give an opportunity to mediate upon the ways of God to man.

But is there anything to consider? Is there any meaning in this visitation which can, without presumption, be fixed upon, by us, as the subject of attention? . . . Has not the whole course of events which take place in the world, a design? But if there are ends to be accomplished by all things, will there not be a relation, an intentional relation, between the means and the ends? . . . Was there ever a calamity in the world, not miraculous, which possessed such a high and solemn moral significance as this pestilence? We

saw an evil, the most insidious and deadly, entering the world by a thousand avenues, and gaining a strength . . . by the modern improvements . . . in the process of distillation.

At this very crisis, there appears in the world, a disease unknown to former times, and it appears as the grand antagonist to the monster, Intemperance.

If this is not providence, what is a providence? If a new species of brain-fever were to appear in the world, and if it made gamblers its principal victims, what more specific and solemn moral would it hold out, than is to be found in this plague of the cholera?

I firmly believe that if there had been no intemperance in the world, this pestilence would not have been in the world. Intemperance has occasioned it, created it, called it into being. Is it too much to say, that it was designed for the check and destruction of the vice in question? . . . it was designed to teach and explain this great doctrine of a providence, to the generation of the thoughtless, the negligent, and skeptical.

The Cholera, I am firmly persuaded, will prevent more suffering than it will occasion. The woes of unrestricted intemperance in this country for ten years, would be far greater than the woes of a ten years' plague . . . I dare not absolutely pray for the removal of this disease, any more than for the removal of many other diseases. I see clearly that the world would sink at once into the ruins of sensual indulgence, if no pain or sickness followed excess.

As the scientific world now recognizes, cholera is an infectious disease which knows nothing of religion. In truth, it is the most secular of diseases. Its *Vibrio* bacteria are spread through shallow wells fed by the periodic overflow and seepage from neighboring cesspools and privies. Accordingly, the disease concentrates in the crowded housing of coastal cities, particularly those dilapidated dwellings with poor sanitation or in those people, such as longshoremen, sailors and

prostitutes whose occupations are conducted on the waterfront.

Aided by more rapid transportation, intensified trade, religious pilgrimages and military campaigns, the germs of cholera spread from their endemic home in the Ganges delta, in 1817, to gain a foothold in Europe in 1827 and the new world in 1832. Its arrival in Europe coincided with an interval of profound social unrest and local famines. The first cholera pandemic proceeded then to entwine itself within the fabric of intensifying social revolution.

The Irish immigrant of the 1827-35 period was the tragic vector who first transported cholera from the hovels of Europe to the harborside tenements of America. And these early Irish refugees, as well as those who shared their waterfront ghettos, were cholera's principal new world victims. The alcoholism, called then intemperance and said to be greater in the immigrant Irish, was then incriminated as the basis for the pestilence. (To quote again the sermon, " . . . if there had been no intemperance in this world, this pestilence would not have been in the world.")

The emergence of cholera in the English-speaking United States accelerated the growing evangelical temperance movement while also heightening the fear that the newly immigrant Irish threatened the jobs, the political stability, the religious beliefs and even the public health of the native New Englanders. It would be another 50 years before certain clergy would speak darkly of Rum, Romanism and Rebellion.

In 1832 the wave of cholera was regularly equated with human sin and an interventionist God. Cholera was proclaimed as the residue of sin, a disorder conferred by God upon those who were dissolute, intemperate, and mind-

less of the virtues of goodness, cleanliness and probity. Death in a cholera hospital was regularly regarded as evidence of a life mispent.

Had the energies behind all of this nineteenth century righteous indignation been invested in better hospital facilities, better epidemiologic inquiry, and better laboratories for proper research into the down-to-earth etiology of cholera, our understanding of the cause and cure might have been sooner achieved. The parallels between cholera, then, and AIDS, now, are uncomfortably close and certainly worthy of thoughtful comparison. AIDS is burdensome enough without our adding the weight of our opprobrium.

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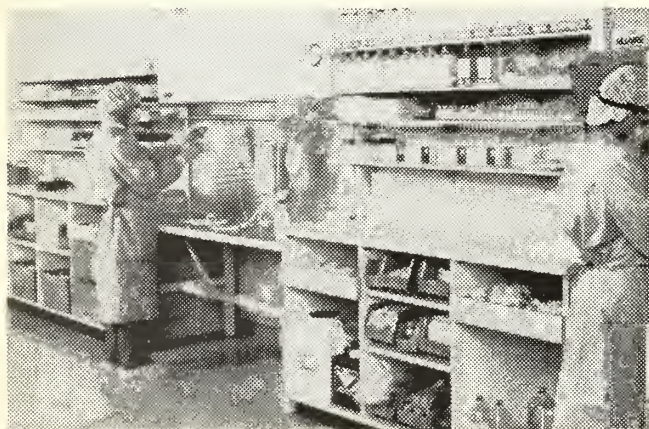
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Heterosexual Behavior and HIV Infection: The New England Behavioral Health Study

Sally Zierler, DrPH
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Charles Carpenter, MD
Kenneth Mayer, MD

... the study is a five year, population based, cohort study. This means that over its duration, people continually enter the study. A subset of these participants, those who have been judged to be at high-risk for HIV infection or who entered the study with serologic evidence of HIV infection, are seen at regular intervals for up to five years.

In 1986, in response to increasing evidence of heterosexual spread of HIV infection in the United States and the unusual proportion of heterosexually active people with AIDS in Rhode Island,¹ we proposed a study to investigate the pattern and determinants of HIV infection among heterosexually active adults. With promises for referral from a supportive network of health care providers and visions of a publicity campaign that was fitting for a presidential candidate we embarked on a quest for three to four thousand heterosexually active women and men who would be willing, if not eager, to be stuck with needles, physically examined and asked to discuss every intimate detail of their sexual practices imaginable and unimaginable as though they were

discussing last night's Celtics' game. The National Institute of Allergy and Infectious Diseases of the National Institutes of Health granted our request and funded what one reviewer noted could be "an administrative nightmare." We named the project the New England Behavioral Health Study (NEBHS), and refer to the outreach component of our HIV testing and counseling program as Project Prevent.

For six months we built our clinic, hired nurses, interviewers, project administrators, data managers and worried whether anybody would want to be in our study. We developed questionnaires, clinical exam forms, follow up protocols and laboratory forms. We gave practice interviews to friends and coworkers who graciously let us draw blood

and counsel them about HIV antibody testing and about preven-

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

CDC: Centers for Disease Control

CODAC: Community Organization for Drug Abuse Control

ELISA: Enzyme Linked Immunosorbent Assay

HIV: Human Immunodeficiency Virus

HTLV: Human T-Cell Leukemia Virus

IUD: Intra-Uterine Device

IV: Intra-Venous

NEBHS: New England Behavioral Health Study

STD: Sexually Transmitted Disease

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tion of HIV infection. By March of 1988 we were open for business. Armed with phlebotomy gear packed in portable ice chests and pages of questions that would make Dr Ruth blush, we announced our presence to the people of Rhode Island,² and waited.

This article tells the story of our experience over the next year and a half. We share this story because we have learned so much about heterosexually active adults in Rhode Island — their sexual, smoking, drinking, drug using, and interpersonal behaviors — behaviors that have bearing on people's risk not only for HIV-related diseases, but for many other diseases that are associated with lifestyles that include multiple sexual partners and use of alcohol, cigarettes and street drugs. Many of these people, and many more like them, are seen by local Rhode Island physicians for primary care, birth control, pregnancy management, and medical management for symptoms of common medical conditions. Some of these people are infected with HIV.

We have also learned a lot about human fear and desperation, about powerlessness and hope. What began as a study has evolved into a compassionate, yet scientifically rigorous, experience of reaching out to the people of Rhode Island who are concerned about the epidemic of HIV infection, for themselves as well as for others. By describing the nature of the information we are gathering and the methods that have worked (and not worked) during this process, we offer a perspective of human sexual life that is only euphemistically and often vaguely discussed in clinical training. In the midst of the horrors of AIDS, the clinician wants to know what to ask, and how to ask, about high risk sexual practices. The New England Be-

havioral Health Study is investigating these issues.

Methods

The overall design of the study is a five year, population based, cohort study. This means that over its duration, people continually enter the study. A subset of these participants, those who are judged to be at high risk for HIV infection or who enter the study with serologic evidence of HIV infection, are seen at regular intervals for up to five years.

Study Population: Anyone at least 18 years old and sexually active with someone of the opposite sex is eligible to be in the study. This description includes bisexual women and men who are currently heterosexually active; HIV serologic status is not part of the eligibility criteria. Most of the people in our study do not have evidence of HIV infection. People enter the study either because a health care provider recommends the protocol or because publicity about the study motivates people to refer themselves. This publicity, distributed broadly throughout Rhode Island, includes a televised public service announcement, print ads in newspapers, brochures, book-marks, matchbooks, posters, and word-of-mouth. Information about the study appears in health care agencies and private practices, bars, libraries, bookstores, college campuses, drug treatment centers, hospitals, community centers, on telephone poles and tee shirts.

Information routinely collected: A list of the type of information that people provide for this study is given in Table 1. In general, the data include laboratory observations from serologic specimens with plans to add urethral and vaginal specimens to the protocol; clinical observations from physical examinations, in-

Table 1. Information routinely collected in the New England Behavioral Health Study.

Demographic information
Age, gender, race, ethnicity
*Socioeconomic status
Sexual practice
Number of sexual partners, sexual preference, contraceptive practices
*Nature of sexual activity, extent of contact with genital secretions, nature of sexual activity with steady, casual and paying partners; nature of sexual activity with HIV infected partner
Medical history
Sexually transmitted diseases
Past and current use of psychoactive drugs, including alcohol
*Viral illnesses, symptoms related to HIV infection, use of therapeutic drugs, reproductive health, genital health, duration of HIV infection
Physical examination
Temperature, skin lesions, presence of adenopathy, thrush, herpes zoster, genital lesions, cervicitis, vaginitis, urethritis, perianal lesions, *Pap smear
Laboratory investigation
HIV antibody by ELISA and confirming Western Blot, HIV antigens (p24 and gp120)
*Hemoglobin level, platelet count, total white blood count, lymphocyte, monocyte, polymorphonuclear cell count, total T-cell number, T helper and T suppressor number, T helper/T suppressor ratio, HTLV-1 antibody, HIV-II antibody, HIV cultures of peripheral leukocytes in semen and cervico-vaginal secretions

*Refers to additional information collected at six month intervals during each follow up visit among participants of longitudinal study.

cluding genital examinations; behavioral observations from self-reported information on sexual practice, alcohol and other drug use patterns, and reported changes in behavior that have bearing on risk of acquiring or transmitting HIV infection; self-reported medical history; and self-reported demographic information.

Protocol schedule: Essentially, two protocols are offered. Everyone in the study is offered the first protocol, and a subset is offered the second. The intent of the first protocol is to assess the proportion of people who enter the study with evidence of HIV infection. We call this initial protocol the seroprevalence study. This component involves screening for HIV antibody and for behavioral risk factors for HIV infection. Typically, an individual is seen only twice during this protocol — the first time for counseling about testing, completion of a brief, self-

administered questionnaire, and HIV antibody testing. About two weeks later, the person returns for test results, post-test counseling, education about risk reduction, and referral to an appropriate health care provider if the HIV counselor or clinician finds a basis for this or the client requests a health care resource. As part of this protocol, a physical examination is offered, but is not required.

The second protocol is a follow-up study of a subset of people who have completed the first protocol. Everyone who has evidence of HIV infection or who reports a recent history suggesting increased risk for acquiring HIV infection is invited to participate in the longitudinal study. Every six months at least until the present study's funding ends in 1992, an individual returns for continual serologic, behavioral, and clinical monitoring. The follow up protocol includes repeated meas-

urement of the information gathered from the first protocol, but the behavioral questionnaire is a lengthy, detailed interviewer-administered set of structured questions about sexual practices since the last visit and other relevant behaviors. The physical and laboratory examinations are more extensive at the follow-up visits, and will include careful genital examinations and specimen collection during the third project year.

Study Personnel: Everyone who works on this study has been touched by the strength and suffering of the people walking in the door for information and guidance. A dynamic tension flows from the desires of our clinicians and counselors to work as caregivers, and the mandate they have to enroll hundreds of people and collect data using a structured, seemingly impersonal format. Juggling the research goals with the day to day clinical and psychosocial demands of the people in the study is a situation ripe for staff "burn-out." The small staff and limited resources have translated into a stretching of roles and assumption of multiple responsibilities. Everyone has worked at some point as babysitter, coach, confidant, counselor, teacher, receptionist and appointment scheduler while also functioning in the roles for which they were presumably hired.

In addition to coping with highly emotionally charged issues, the staff is asked continually to adapt to protocol changes in response to increasing knowledge about the epidemic and its management, such as developments in diagnostic capabilities, treatment modalities and identification of risk factors.

Recruitment Strategies: Our goal has been to recruit a few thousand people so that we would be able to describe statistically

valid and generalizable observations on heterosexual behaviors and HIV transmission. This goal has had to be revised because of obstacles that are inherent in the nature of the AIDS epidemic. While the general public has been barraged with information about AIDS, myths still abound. Some people continue to believe that only homosexual men or intravenous drug users become infected. Others are too afraid to be tested. With HIV infection perceived as a death sentence, fear is an extremely potent obstacle to recruitment of study volunteers. Traditional gender roles, religious and cultural proscriptions against open discussion of sex and language barriers combine to limit the numbers of participants from minority communities.

Some obstacles to effective recruitment relate less to attitudes and beliefs about AIDS than to the study protocol. Multiple visits, lengthy questionnaires in the follow-up period, and probing about stressful topics cause some participants to discontinue participation in the study. Given that HIV antibody testing is required for study participation, there is concern regarding confidentiality and limits of data accessibility.

In consideration of our ambitious recruitment goals in the context of these obstacles, two major strategies were developed that consisted of outreach to the provider community and advertising to the general public for self-referral.

We discovered that generating referrals for the study was a little

like running for an elected office: nonstop presentations, press releases, mailings, open houses, and lots of hand shaking. Before the grant proposal was submitted, we consulted with many clinicians and administrators from health agencies to elicit their support and participation. After the grant was awarded, meetings too numerous to count were organized to develop specific referral protocols. Initially, at least ten different Institutional Review Boards, each with unique requirements, agreed to provide people and the space to enroll them. Many more individuals have met with us to discuss procedures for referral to some of these sites. We have met with clinical staff from virtually every Brown University teaching hospital at one time or another, some on many occasions. The Rhode Island Health Department, drug treatment programs including Marathon House and CODAC, and community agencies such as the Urban League and the Hispanic Social Services Association have invested hours of telephone and personal meeting time to discuss recruitment challenges.

For the general public we designed a print ad campaign which has appeared in a variety of newspapers. With the help of donated efforts from Brown students and WJAR Channel 10, we produced a television public service announcement that continues to run on local television stations. Recently, we have introduced a dramatic radio broadcast. In addition to these media ventures,

through which we hoped to become familiar and well-seeded in the minds of a diverse audience, we have also distributed AIDS education and information about the study on brochures, posters, bookmarks and matchbooks.

Ethical Protocol: The study protocol asks a disparate group of individuals to confront their risk of exposure to a deadly virus, and to travel to a place which for some may be a remote part of the state (Pawtucket) to share this information with complete strangers. Given the deeply personal nature of the contribution we are asking from people, it has been essential that consent to participate be truly informed. The study protocol is only the skeleton for a fully fleshed ethical policy, where confidentiality is a major focus. Our coding system is designed so that no one outside of the study staff can link data with any personal identifiers. Study participants must provide written authorization for disclosure of any information related to their medical or laboratory records, and only after discussion with their study counselor about the possible effects of disclosure.

Our coding system is designed so that no one outside of the study staff can link data with any personal identifiers.

Most of all, the people in our study are not merely research subjects. We are continually grateful for their willingness to share their experience. In return, we offer counseling and the opportunity for discussion of concerns that may be outside the realm of the epidemic. No one leaves the study sites without information, and when needed, appointments for triage to medical, social and psychological services.

Acknowledgements

We are indebted to the staff of the New England Behavioral Health Study:

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Diane Campbell, secretary;

Priscilla Velentgas and Jennie Hoffman, research assistants;

And to the women and men who generously share their struggle and hope by participating in this study.

Results

Recruitment experience: As of September 1, 1989, 576 individuals have entered the New England Behavioral Health Study. Enrollment began slowly with two study participants entering in February of 1988 and has grown steadily to 40-50 new enrollees each month.

Individuals entering the study are either referred by a health care provider or are self-referred. Figure 1 shows that among those referred by a provider, physicians (both community and hospital based) account for the largest number of referrals. This is true regardless of HIV status. Approximately 60% of the people who were HIV-infected at the time of enrollment into the study were referred by a physician.

Among those entering the study on a self-referred basis, slightly less than half reported hearing about the study from a friend or from the AIDS hotline, while the remaining 56% reported learning about us from television and radio public service announcements or from printed advertisements.

As noted earlier, recruitment occurs in numerous sites in Rhode Island and Southeastern New England. Table 2 describes the proportion of people seen at different study locations. Over half of those enrolled in the study were seen at the clinic in Memorial Hospital. An additional 28% were recruited at methadone maintenance clinics (CODAC and in New Bedford Area Center for Human Services), and another 12% at HIV and STD clinics in Rhode Island hospitals.

Detailed descriptions of the demographic, medical and sexual characteristics of the study population appear in Table 3. The cohort consists mostly of people between the ages of 24-44 with the majority classifying themselves as

Table 2. Locations in Rhode Island and Southeastern Massachusetts for Enrollment into the New England Behavioral Health Study

Location	Number Enrolled	Per Cent
Memorial Hospital	312	54
New Bedford Area Center for Human Services	116	20
CODAC	45	8
St. Joseph Hospital, STD Clinic	39	7
Mobile Van (Providence city limits)	34	6
Miriam Hospital	17	3
Rhode Island Hospital	10	2
Other	3	<1
Total	576	100%

white. Forty-two per cent of those enrolled reported a history of intravenous drug use, while 36% reported having had a prior sexually transmitted disease.

HIV seroprevalence in this population has remained fairly stable over the past year. Currently, 18% of the study population has evidence of infection. It is important to note that the frequency of HIV infection in the study cohort is a reflection of our recruitment strategies, which overselect for individuals who have engaged in high-risk behaviors. In other samples in Rhode Island, the estimate of prevalence of HIV infection varies from .015% in blood donors, about 4% in the population seeking testing at the Health Department's counseling and testing sites, and 18% among prisoners.³

As of September 1, 1989, 576 individuals have entered the New England Behavioral Health Study.

In fact, over three quarters of study participants perceived themselves to be at increased risk of HIV infection when entering the study, and most others did not know whether or not they were at increased risk. While a small percentage of individuals reported having a current sexual partner who is HIV infected, approximately 30% of the women and 16% of the men did not know if

their current partner had HIV infection. Almost half of the people reported that they had been sexually active in the last year with someone they knew was at high-risk of being HIV infected. For the overwhelming majority, the high-risk behavior of these sexual partners was use of intravenous drugs.

Most of the people enrolled in our study are exclusively heterosexual. Over their lifetimes, two-thirds of our population reported having had more than 10 sexual partners. During the year prior to their enrollment, approximately half reported having two or more different sexual partners. Among those reporting at least one sexual partner in the last year, a variety of birth control methods were used. Frequency of condom use during the year prior to enrollment was similar for women and men, with over half reporting that they never used condoms. Only 7% of the study group reported using a condom during all sexual encounters. Most study participants reported that, at least once during their sexual encounters in the six months prior to enrollment, no effective method of birth control or HIV prevention had been used.

Among the HIV infected people, the majority reported multiple risk factors. Table 4 lists the possible modes of transmission of HIV infection in the current study population. Given the prevalence of intravenous drug use

Table 3. Medical, Sexual, and Demographic Characteristics of Heterosexual Cohort at Entry, March 1988- September 1989, by gender.

Characteristic	Women		Men		Total	
	n	%	n	%	n	%
Age:						
18-24	53	21%	55	18%	108	19%
25-34	137	54	133	44	270	49
35-44	51	20	91	30	142	26
45+	11	4	22	7	33	6
Total	252	—	301	—	553	—
Race:						
White	205	81%	224	74%	429	77%
Black	15	6	14	5	29	5
Latino	16	6	33	11	49	9
Other	16	6	31	10	47	9
Total	252	—	302	—	554	—
HIV Status:						
Antibody Positive	53	21%	49	16%	102	18%
Antibody Negative	199	79	253	84	452	82
Total	252	—	302	—	554	—
History of IV Drug Use:						
Yes	93	37%	137	45%	230	42%
No	159	63	165	55	324	58
Total	252	—	302	—	554	—
Self-perception of Risk for HIV Infection:						
Increased Risk	200	79%	220	73%	420	76%
No Risk	18	7	42	14	60	11
Don't Know	29	12	35	12	64	11
Has AIDS	5	2	4	1	9	2
Total	252	—	301	—	553	—
History of STDs:						
No	164	65%	189	63%	353	64%
Yes	87	35	112	37	199	36
Total	251	—	301	—	552	—
Current Partner HIV-infected:						
Yes	17	7%	23	8%	40	7%
No	160	64	229	76	389	71
Don't Know	71	29	50	16	121	22
Total	248	—	302	—	550	—
Sexual Preference:						
Exclusively Heterosexual	228	90	254	85	482	88
Not Exclusively Heterosexual	10	4	26	9	36	6
No Sex in Last Year	14	6	20	7	34	6
Total	252	—	300	—	552	—
# Sex Partners in Last Year:						
0	14	6%	21	7%	35	6%
1	123	49	105	35	228	41
2-9	100	40	152	50	252	46
10+	12	5	23	8	35	6
Total	249	—	301	—	550	—
# Lifetime Sexual Partners:						
1	10	4%	2	1%	12	2%
2-9	102	41	72	24	174	32
10+	138	55	225	75	363	66
Total	250	—	299	—	549	—
Sex with High Risk Person in Last Year:						
No	133	53%	185	61%	318	57%
Yes, with IV Drug User	97	38	89	29	186	34
Yes, with other	22	9	28	9	50	9
Total	252	—	302	—	554	—
Age at First Sexual Experience:						
6-13 years	29	11%	71	23%	100	18%
14-17	143	57	168	56	311	56
18-21	75	30	57	19	132	24
22+	5	2	5	2	10	2
Total	252	—	301	—	553	—
Contraceptive Use in Last Six Months:						
Condom (n = 512)	94	40%	125	45%	219	43%
Diaphragm (n = 509)	16	7	14	5	30	6
Vaginal Foam, etc. (n = 509)	20	9	17	6	37	7
Oral Contraceptive (n = 511)	47	20	62	22	109	21
Rhythm (n = 511)	20	8	13	6	33	8
Withdrawal (n = 509)	37	16	55	20	92	18
IUD (n = 507)	3	1	7	3	10	2
None (n = 510)	103	44	152	55	255	50

among the HIV infected people, it is likely that most, if not all of the intravenous drug using infected individuals acquired their infection from sharing needles.

... In Rhode Island, the estimate of prevalence of HIV infection varies from 0.015% in blood donors, about 4% in the population seeking testing at the Health Department's counseling and testing sites, and 18% among prisoners.

Among infected men, 8% reported a history of bisexuality only, while an additional 24% reported a history of both bisexuality and intravenous drug use. Twenty per cent of the people with infection reported that their only risk factor was heterosexual sex. Women were nearly twice as likely to attribute their infection to heterosexual transmission compared to men (26% vs. 14%, respectively). Most of the individuals in this category reported heterosexual activity with an intravenous drug user, a known HIV infected person, or a bisexual man in the year prior to enrollment. One person indicated that he had received a blood transfusion before 1985 that he suspected was contaminated with HIV.

Discussion

To date, nearly 600 people have given important information to help us evaluate the potential for spread of HIV infection in the Rhode Island area. In return, we have provided education, compassionate counseling and condoms — lots of condoms. Together, we hope to increase understanding of how this virus is heterosexually transmitted and what the characteristics are of the people who are most likely and

least likely to become infected after exposure to the virus.

Some of this understanding is already evident. Heterosexual transmission of HIV in Rhode Island is no longer hypothetical. It is a reality. Spread of the virus is bidirectional, going from men to women and from women to men. Because these data are based on self-reports in the context of considerable stigma attached to male homosexual activities and to drug use, the possibility exists that some of the individuals may be misrepresenting their exposure histories. However, many of the infected individuals are part of the longitudinal study, and have developed a trusting relationship with the clinical staff. During each six month visit, the clinicians repeat questions about high-risk behaviors to assess the reliability of reporting. To date, no one in the follow-up study has suggested that the original classification of mode of transmission should be altered.

... the current educational initiatives to prevent the spread of HIV transmission do not seem to be effective in changing behaviors.

Our data also suggest the high potential for spread of HIV among

the heterosexual community in Rhode Island. Among infected people who are also intravenous drug users, approximately one-third report having had more than one sexual partner in the last year and there is a widespread lack of condom use in this population.

Another disturbing, yet clarifying, finding from these data is that the current educational initiatives to prevent the spread of HIV transmission do not seem to be effective in changing behaviors. Approximately half of all study participants, including infected and uninfected individuals, report never using a condom in the last year, and only 7% report always using a condom. In response to this observation, we have introduced a set of questions to a subset of the study cohort to investigate reasons why people choose not to use condoms once they have been educated about the risks of transmission of HIV infection.

Although this is a natural history study in that we are observing the progression and transmission of HIV infection over time, we do not feel that it is ethical to be non-interventional. Thus, we appraise all HIV-infected study participants of the need to seek ongoing medical attention and to consider antiretroviral chemotherapy if

Table 4. Probable mode of transmission of HIV infection among heterosexually active participants in the New England Behavioral Health Study

Reported high risk exposures	Women (%)	Men (%)	Total (%)
Heterosexually active and intravenous drug use	39 (74)	25 (51)	64 (63)
Heterosexually active only	14 (26)	7 (14)	21 (20)
Among men, bisexually active and intravenous drug use	—	12 (24)	12 (12)
Among men, bisexually active	—	4 (8)	4 (4)
Blood transfusion before 1985	0 (0)	1 (2)	1 (1)
Total	53 (100)	49 (100)*	102 (100)

*column may not add to 100% because of rounding error

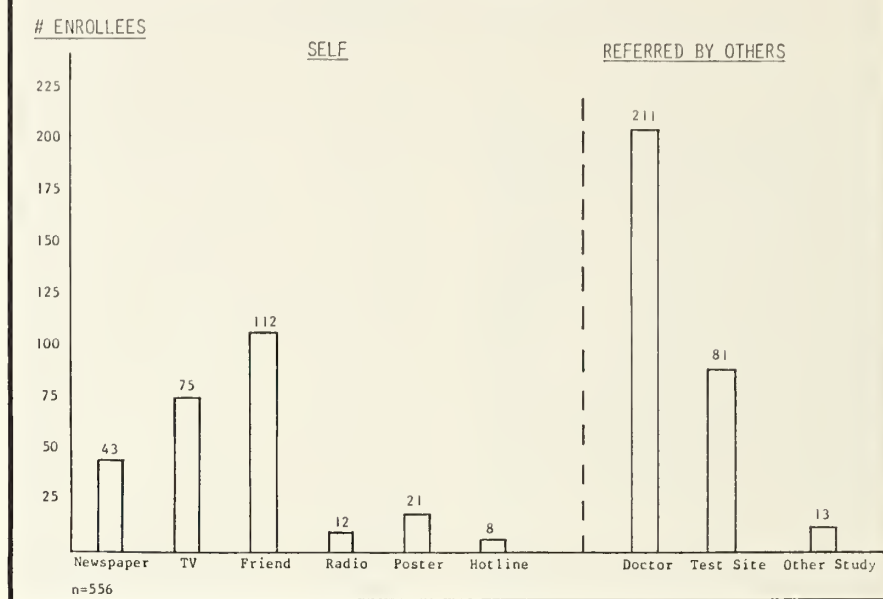
their T helper lymphocyte counts are low. We also continue to educate uninfected people in ways to avoid HIV infection. Thus, we must be careful about generalizing about behaviors that we observe in the study population. We do not assume that study volunteers necessarily are identical to those individuals who do not choose to participate in the study.

Recently, we received additional funding to implement two new protocols. The first, funded by the Centers for Disease Control, enables us to look more closely at heterosexual couples where one individual is HIV infected and the other has no evidence of infection. From these HIV serologically discordant couples, we hope to learn more about the factors involved which enhance or discourage transmission of HIV between sexual partners.

People enrolled in the couples' study are seen three to four times a year. In addition to the basic protocol, the couples provide additional behavioral data that are specific to their relationship with their sexual partner who is also enrolled. Additionally, they receive free screening for sexually transmitted diseases and provide the study with cervico-vaginal or semen specimens for immunologic investigations to identify cofactors that influence infectiousness of genital secretions.

A second protocol, about to be implemented, involves expansion of screening for the most common sexually transmitted diseases. Provided that federal funding sources are sufficient, testing will be conducted for chlamydia, gonorrhea, syphilis and herpes. In addition, women will receive Pap smears. From this additional information, we hope to learn more about possible biologic and virologic cofactors involved in the sexual transmission

Figure 1. Referral Source for NEBHS Participants, March 1988 — August 1989.



of HIV. All people with evidence of genital pathology will be referred to an appropriate health care provider for treatment.

Based on current enrollment figures, we expect to have enrolled 1500 people in the seroprevalence study by the end of our recruitment in December, 1991. Currently, approximately 200 people are being followed up at least every six months for the longitudinal study, and the aim is to double the size of this cohort.

The New England Behavioral Health Study is one of a few nationally funded studies that is investigating heterosexual spread of the human immunodeficiency virus. It is the largest study addressing this question in the northeast United States outside of the New York metropolitan area. We expect that as the study population increases, we will be able to identify important biologic, virologic and behavioral cofactors that affect transmission of and susceptibility to this infection. Furthermore, together with the many health care providers who work with us to educate, counsel, and care for those enrolled in our study, we have been given an un-

usual opportunity to have an impact on the public health of the people in Rhode Island and Southeastern Massachusetts.

Another initiative currently under way is to increase enrollment of individuals from Hispanic and African-American communities, not only because these communities typically are underserved by the health care system, but also because of the disproportionate representation of heterosexual people with AIDS from these ethnic groups.

References

- 1 Rhode Island AIDS Alert, Office of Disease Control, Rhode Island Department of Health, Summer, 1989.
- 2 Press Release, "New heterosexual AIDS-related study", April 13, 1989.
- 3 "AIDS in Rhode Island, 1986-88: A demographic profile" Office of Health Statistics, Rhode Island Department of Health, April, 1989.

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Work-up of the Patient with HIV Infection

Alvan E. Fisher, MD

... the sexual history (of patients) should include a discussion of the number and sex of partners, contact with prostitutes or known IV drug users, and specific sexual practices.

The management and evaluation of patients with HIV infection requires a multidisciplinary effort. Medical evaluation can only occur after identification of infection; this evaluation must include attention to social and psychosocial factors. After the evaluation, education, observation, and intervention follow.

Identification of HIV Infection

Identification of patients with HIV infection begins with awareness by the physician of the risk behaviors associated with HIV transmission. The medical history needs to include a full and free-ranging discussion of sexual and drug history. Heterosexual contact has become increasingly important in HIV transmission; the sexual history should include a discussion of the number and sex of partners, contact with prostitutes or known IV drug users, and specific sexual practices. The

geographical areas where sexual contacts have occurred is very important because of the highly variable prevalence of HIV infection.¹ The use of barrier techniques with or without spermicide will have bearing on the risk of acquisition of HIV infection as well. A complete drug history must include the obvious questions about use of intravenous drugs and needle-sharing. Occupational exposure by health care workers through needle puncture accidents is common but is still rarely associated with HIV transmission.²

Certain clinical symptoms or findings should suggest the possibility of HIV infection even without a history of high-risk behavior. These include the presence of lymphadenopathy, oral candidiasis or hairy leukoplakia as well as a history of unexplained fevers or weight loss.³ Unexplained thrombocytopenia may occur prior to other laboratory or clinical findings of HIV infection.⁴ Any of these findings should be considered an indication of underlying HIV infection and should lead to a discussion of HIV testing.

Counseling prior to testing involves encouraging those pa-

tients with any risk, history, symptom, or sign suggestive of HIV infection to consent to HIV testing. Concerns about confidentiality and discrimination have to be addressed as do the advantages of early identification and early intervention. The recently reported benefits of early treatment with the antiretroviral drug zidovudine is a major inducement to early testing and should be discussed especially with those unwilling or uncertain about testing.

An appointment for post-test counselling and discussion of results is necessary;⁵ an in-person meeting of adequate time to discuss the significance of both positive or negative HIV test results is advisable to avoid misconceptions (especially for those with negative results) and to begin further evaluation and intervention

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

CMV: Cytomegalovirus

HIV: Human Immunodeficiency Virus

HSV: Herpes Simplex Virus

PCP: *Pneumocystis carinii* Pneumonia

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(for those with positive results). It is inappropriate to give such information by telephone as it is impossible to predict an individual's response to these results.

Medical Evaluation

After identification of HIV infection, a full medical, social, and psychological evaluation is necessary. The medical evaluation includes obtaining a history of symptoms related to HIV infection or its complications. The systemic symptoms of weight loss, fever, and night sweats can be related to progressive HIV infection itself or be the harbinger of HIV-related complications such as opportunistic infections or malignancies.⁶ Skin disorders, headache, disturbances of thinking, vision, respiratory or gastrointestinal function may be the first symptom of complications of HIV infection. Prior exposures to other infectious diseases may complicate the management of HIV infection. Herpes simplex virus, tuberculosis⁷ and syphilis⁸ may all reactivate after HIV-related immunosuppression and may require chemoprophylaxis. Hepatitis B may increase the risk of liver disease in patients with HIV infection.

An appointment for post-test counselling and discussion of results is necessary . . . it is inappropriate to give such information (ie, blood test for HIV) by telephone as it is impossible to predict an individual's response to these results.

Psychosocial dysfunction is common in patients with HIV infection⁹ and can be detected and discussed during history taking. Family ties may be strained or nonexistent in many patients at risk for HIV infection. Symptoms of anxiety, depression, or

denial should be discussed as should referral for intervention if necessary. Many patients benefit from HIV-related support groups.

During the physical examination special attention must be given to areas that are frequently affected by complications of HIV infection. The most important of these are the oropharynx and the skin. Multiple complications of HIV infection occur in the oral cavity;¹⁰ most of these can be presumptive evidence of progression of HIV infection from early to more advanced stages. Oral candidiasis and oral hairy leukoplakia are the most common of these and usually occur when significant immunosuppression has occurred.^{11, 12} Oral herpes simplex infection may occur at any time but may become refractory to therapy with progressive immunosuppression. Kaposi's sarcoma frequently presents with oral lesions or occurs concurrently on the skin and in the oral cavity.¹³ Many other HIV related complications affect the skin such as molluscum contagiosum, eczematous dermatitis, herpes simplex infection, and herpes zoster. The recurrent or protracted nature of these lesions is directly related to HIV induced immunosuppression and may be a clue to progression of the immunosuppression. The remainder of the exam must include close attention to the presence of lymphadenopathy, hepatomegaly or splenomegaly, as well as the status of cardiopulmonary function. Careful genitorectal examination looking for the presence of prior or current sexually transmitted disease (including herpes simplex) completes the general examination. Perianal infection with HSV is frequently misidentified by both patients and physicians but is very common and readily identified clinically or by viral culture.¹⁴

Lymphadenopathy is a common finding in patients with HIV infection and may indicate more rapid progression to AIDS;¹⁵ the lymph nodes generally are diffuse, small, soft and nonfixed. Lymph node biopsy is usually unnecessary unless there is clinical suspicion of either a complicating infection or malignancy as with unexplained constitutional symptoms when specific nodes are greatly enlarged, fixed or firm.

The laboratory testing establishes baseline results in such tests as complete blood count, platelet count, biochemistries (hepatic, renal, metabolic), chest radiography, and pulmonary function testing. Anemia, leukopenia and elevated erythrocyte sedimentation are seen in patients with more advanced HIV infection and may relate to progression of HIV infection.¹⁶ Thrombocytopenia frequently occurs earlier and may be both quite severe and responsive to zidovudine or other therapies. Specific tests of past infections that may reactivate due to HIV infection include serological testing for CMV, toxoplasmosis, syphilis, and hepatitis B. Tuberculin testing may reveal evidence of occult past infection with tuberculosis; cutaneous anergy is present in many patients (especially those with more advanced immunosuppression).

Evaluation of immune function is primarily accomplished with measurement of absolute counts of T4 and T8 lymphocytes.¹⁷ The T4 lymphocyte count is the most important as it reveals both the current status of immune function and the immediate and long-term prognosis of the patient. The T4 lymphocyte is the target cell of HIV infection and is more frequently infected with HIV than other white blood cells.¹⁸ A diminished T4 lymphocyte count (less than 200) has been clearly

shown to correlate with an increased risk of HIV-related opportunistic infection and progression of HIV infection.^{16, 19} A normal level of T4 lymphocytes (greater than 500) correlates with a negligible short-term (one to two year) risk of such complications. Prophylaxis for *Pneumocystis carinii pneumonia (PCP)* as well as intervention with zidovudine or other antiretroviral drugs is based primarily upon the level of T4 lymphocytes especially in asymptomatic patients.²⁰

The systemic symptoms of weight loss, fever, and night sweats can be related to progressive HIV infection itself or be the harbinger of HIV-related complications such as opportunistic infections or malignancies.

The HIV p24 antigen is considered a marker for progression of HIV infection.²¹ This antigen is generally nondetectable during the asymptomatic stage but may become detectable as HIV infection progresses. Quantification of p24 antigen can be used to monitor progression of HIV infection as well as response to antiretroviral therapy. The serum beta-2-microglobulin, a nonspecific marker of immune function, also correlates with progression of HIV infection. The combination of diminishing T4 lymphocyte count, rising p24 antigen and beta-2-microglobulin levels may be the strongest current laboratory evidence of progression of HIV infection.¹⁶

Patient Education

Prevention of transmission of HIV needs to be discussed with the patient; contraception and "safer sex" techniques need to be described in detail to avoid misunderstanding. Voluntary or anonymous notification of past sexual

or drug sharing partners can be discussed at this time as well.

If patients learn about the natural history and complications of HIV, unnecessary fears over unrelated or trivial problems can be avoided. In addition the patient can help the physician in the early recognition of complications. Patients need to be instructed in techniques of self care to avoid illness of further complications.²² Many volunteer groups are available across the United States to provide education and support to individuals with HIV infection; printed materials and support groups can be very helpful for many patients.

The health care provider should monitor the patient for progression of HIV infection so that appropriate and early intervention can be accomplished. There is an increasing volume of evidence that patients survive longer if major complications are evaluated and treated aggressively as early as possible. Early intervention with antiretroviral drugs results in delay of progression to AIDS.²³ Prophylactic therapies to avoid AIDS-related complications have become routine for PCP and may enlarge in scope in the next few years. Patients who develop subtle signs or symptoms of complications such as low grade fever or mild cough, decreased exercise tolerance, unexplained rapid weight loss need an aggressive diagnostic approach to detect AIDS-related complications.

The management and evaluation of patients with HIV infection is similar to that of other chronic diseases involving identification, examination, education and observation and can be accomplished by the patient's primary health care provider without other referral until or unless complications ensue. An understanding of the natural history of HIV infection enables both health care

provider and patient to participate in this management.

References

- Jaffe HW, et al. Acquired immune deficiency syndrome in the United States: the first 1000 cases. *J Infect Dis* 1983;148:339-45.
- Marcus R, et al. Surveillance of health care workers exposed to blood from patients infected with the human immunodeficiency virus. *N Eng J Med* 1988;319:118-23.
- Lang W, et al. Clinical, immunologic, and serologic findings in men at risk for acquired immunodeficiency syndrome: The San Francisco Men's Health Study. *JAMA* 1987;257:326-330.
- Abrams DI, et al. Antibodies to Human T-Lymphotropic Virus Type III and development of the Acquired Immunodeficiency Syndrome in homosexual men presenting with immune thrombocytopenia. *Ann Int Med* 1986;104:47-50.
- Sherer R. Physician use of the HIV antibody test: the need for consent, counselling, confidentiality and caution. *JAMA* 1988;259:1861-2.
- Jaffe HW, et al. The acquired immunodeficiency syndrome in a cohort of homosexual men: A six-year follow-up study. *Ann Intern Med* 1985;103:210.
- Chaisson RE, Slutkin G. Tuberculosis in patients with human immunodeficiency virus infection. *J Infect Dis* 1989;159:96-100.
- Johns DR, et al. Alteration in the natural history of neurosyphilis by concurrent infection with human immunodeficiency virus. *N Eng J Med* 1987;315:1569-72.
- McArthur JC. Neurologic manifestations of AIDS. *Medicine* 1987;66:407-437.
- Greenspan JS, et al. Diagnosis and management of the oral manifestations of HIV infection and AIDS. *Infect Dis Clin N Am* 1988;2:373-85.
- Lupton GP, et al. Oral hairy leukoplakia: A distinctive marker of human T-cell lymphotropic virus type III (HTLV-III) infection. *Arch Dermatol* 1987;123:624-628.
- Klein RS, et al. Oral candidiasis in high-risk patients as the initial manifestation of the acquired immunodeficiency syndrome. *N Eng J Med* 1984;311:354-358.
- Lumerman H, et al. Oral Kaposi's sarcoma: A clinicopathologic study of 23 homosexual and bisexual men from the New York Metropolitan area. *Oral Surg* 1988;66:711-16.
- Kalb RE, et al. Chronic perianal herpes simplex in immunocompromised hosts. *Am J Med* 1986;80:486-90.
- Mathur-Wagh U, et al. Longitudinal study of persistent generalized lymphadenopathy in homosexual men: Relation to the acquired immunodeficiency syndrome. *Lancet* 1984;1:1033-1038.
- Moss AR, et al. Seropositivity for HIV and the development of AIDS and ARC: Three year follow-up of the San Francisco General Hospital cohort. *Br Med J* 1988;296:745-50.
- Goedert JJ, et al. Effect of T4 count and cofactors on the incidence of AIDS in homosexual men infected with human im-

munodeficiency virus. JAMA 1987; 257:331-334.

¹⁸ Ho, et al. Quantitation of Human Immunodeficiency Virus Type III in the blood of infected persons. N Eng J Med 1987; 331:1621-1625.

¹⁹ Polk, et al. Predictors of the acquired immunodeficiency syndrome developing in a cohort of seropositive homosexual men. N Eng J Med 1987;316:61-66.

²⁰ Center for Disease Control. Guidelines for prophylaxis against Pneumocystis carinii pneumonia for persons infected with human immunodeficiency virus. MMWR 1989 Jun 16;38 Suppl 5:1-9.

²¹ Lange JMA, et al. Persistent HIV antigenemia and decline of HIV core antibodies associated with transition to AIDS. Br Med J 1986;293:1459-1462.

²² Lovejoy, et al. Self-Care behaviors and informational needs of seropositive homosexual/bisexual men. J AIDS 1988;1:155-161.

²³ Fischl MA, et al. The efficacy of azidothymidine in the treatment of patients with AIDS and AIDS-related complex. N Eng J Med 1987;317:185-191.

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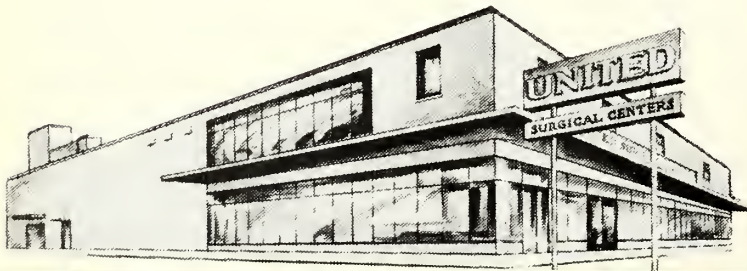
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AMA's Guidelines on HIV Blood Test Counseling

Robert C. Rinaldi, PhD
John J. Henning, PhD

... medical literature contains little in the way of specific guidelines to conduct this (HIV antibody testing) counseling.

This manuscript provides physicians with a brief outline of pretest and post-test counseling to accompany HIV testing.

HIV Blood Test Counseling

The impact of human immunodeficiency virus (HIV) disease on the health care system is increasing. Specialized centers alone are unable to provide all required services. Physicians and other health professionals will encounter a growing number of concerned individuals and family members who need counseling about possible exposure to HIV.

Although counseling related to HIV antibody testing has been widely recommended,¹⁻³ the medical literature contains little in the way of specific guidelines to con-

duct this counseling. The following provides a brief outline of some essential elements required to conduct HIV antibody blood test counseling.

Pretest Procedures

During the pretest session the physician must provide information about HIV, AIDS, and the test, conduct a sex and drug history, and provide counseling. The patient should be told about the virus, HIV related diseases, routes of transmission, and methods of reducing the risk of infection. This can be accomplished through a variety of mediums including videotape, audiotape, printed matter, group lecture, and one-to-one interaction.⁴

The pretest session also must include a patient history of sexual behavior and drug use. The physician should use frank, nonjudgmental, open-ended questions to determine the patient's risk of HIV infection. The physician must be sure that the patient understands the words being used.

Discussing sexual behavior is difficult for many patients and physicians. The interview style and terminology used should be

tailored to suit the comfort of the individual patient and physician. The patient's sexual orientation is less important than the specific sexual practices in which he or she engages.

Discussing drug use with patients also may be difficult. However, information on intravenous drug use and needle sharing is essential. A full drug use history including substances such as alcohol and marijuana also can be helpful.

Pretest counseling should include discussion of medical, psychological, and social implications of the HIV antibody blood test. Specific recommendations for behavior change must be based on the physician's assessment of risk. Finally, the physician can assist the patient in deciding whether or not to be tested.

Essential elements of the pretest counseling session include:

- Ask directly why the patient believes he/she needs to be tested.

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

HIV: Human Immunodeficiency Virus

Drs Rinaldi and Henning are on the staff of the American Medical Association's Group on Science and Technology. This manuscript is based upon the AMA publication entitled, "HIV Blood Test Counseling: AMA Physician Guidelines." The authors can be reached at AMA, 535 N Dearborn St, Chicago, IL 60610.

- Explain that the test determines the presence or absence of antibodies to the virus.
- Discuss the meaning of a positive test result: The individual is infected and assumed contagious but does not necessarily have AIDS.
- Discuss the meaning of a negative test result: An individual is not currently demonstrating infection but is *not* "protected" against the virus.
- Discuss the possibilities of false-positive or indeterminate results.
- Discuss ways to modify behavior to reduce risks.
- Discuss the confidentiality of test results in relation to office/clinic procedures and state reporting requirements.
- Discuss potential benefits of anonymous testing.
- Discuss the stress often related to waiting for test results and possible reactions to learning results (eg, depression and anxiety).
- Discuss potential negative social consequences of being tested and/or being seropositive (employment, housing, insurance, and personal relationship ramifications).
- Assist the patient in making a decision about testing.
- Obtain consent before voluntary testing is conducted (local statutes pertaining to adults and minors should be consulted).
- Make an appointment for a return face-to-face visit to give and discuss test results.

Post-test Counseling

Disclosure of the test result is best done at the beginning of the post-test session in a direct manner. Many patients anxiously anticipate the test result and are eager to learn the findings. After the result is disclosed, the patient should be encouraged to express

feelings. Repeating the patient's remarks and labeling his or her underlying feelings is often helpful.

Reporting a positive result can be difficult. If the patient had predicted a positive result during the pretest counseling session, the physician might say, "Well your prediction was right. Your tests show that you have the virus." Although it is important to be honest and straightforward in reporting a positive result, it is equally important to give the seropositive patient hope. Quoting the annual percentage of seropositive individuals who actually become ill (approximately 7% to 10% per year) and mentioning the ongoing scientific search for effective treatments and vaccines might prove helpful.

The physician must assess the patient's understanding of the result by asking a question such as "Now that you know you are antibody positive (or negative), what does this test result mean for you?" The physician must help the patient understand and assimilate the information. A review of the information conveyed in the pretest session should be conducted.

When the result is negative, the patient's understanding of how to prevent future infection must be assessed. When the result is positive, the patient must be advised on how to avoid infecting others. He or she must understand that infection is probably lifelong but that having a positive antibody test alone does not mean one has AIDS. It is also important to communicate to seropositive individuals that they are probably infectious to others by the established routes of transmission and that there is currently no way to predict with certainty when and if clinical symptoms will develop. Antibody-positive persons should be told:

- Do not donate blood, semen, or body organs.
- Employ what have come to be known as "safer sex practices."
- Do not share personal hygiene items (eg, razors, toothbrushes).
- Inform physicians and dentists of serologic status.
- Encourage sexual partners and needle contacts to seek evaluation and serologic testing.

The physician must be sensitive to the wide range of psychological reactions possible when the test result is given. For seronegative patients, an immediate reaction of surprise and relief may occur, followed by an overall reduction of psychological distress and anxiety. Seropositive individuals may react with expression and disbelief, anger, fear, guilt, or self-recrimination. Clinical depression often occurs among those testing positive for HIV antibody.⁵⁻⁶ In some, the depression may lead to suicidal thoughts or attempts.⁷

Seropositive patients sometimes require repeated sessions, supportive services, and monitoring of psychological functioning. A psychiatric referral should be made for patients who require assistance in adapting to current conditions or managing feelings of depression or anxiety beyond what the primary care physician can offer. A patient may also benefit from counseling hotlines, HIV support groups, and/or psychotherapy. A schedule to monitor medical status must be determined as well.

The post-test session also should include an assessment of the patient's commitment to altering high-risk behaviors. The physician must work with the patient to promote behavior change by reiterating routes of transmission, discussing risks, and high-

lighting methods of risk reduction.

In summary, essential elements of the post-test counseling session include:

- Provide the test result.
- Allow the patient to express feelings and reactions.
- Assess the patient's understanding of the test results.
- Review routes of transmission.
- Assess the patient's psychological condition.
- Recommend psychiatric follow-up when appropriate.
- Assess risk behavior and commitment to risk reduction strategies.
- Recommend medical follow-up.
- Recommend additional support services as needed.

Conclusion

The need for HIV antibody blood test counseling has been widely acknowledged.^{1,2} Physicians must be prepared to provide such services for their patients. The brief guidelines presented here serve as an outline for HIV antibody blood test counseling to patients.⁸

References

- ¹ Board of Trustees: (Report LLL) Progress in the prevention and control of AIDS. Annual meeting, American Medical Association, Chicago, IL, June 1988.
- ² Perry SW, Markowitz JC: Counseling for HIV testing. *Hosp Comm Psychiatry* 1988; 39:731-738.
- ³ Henry K, Maki M, Crossley K: Analysis of the use of HIV antibody testing in a Minnesota hospital. *JAMA*. 1988;259:229-232.
- ⁴ *AIDS counseling and HIV-antibody testing: A position paper*. Coalition for AIDS prevention and education. Washington, DC, American Psychological Association, 1987.

⁵ Faulstich ME: Psychiatric aspects of AIDS. *Am J Psychiatry* 1987;144:551-556.

⁶ Miller D: HIV counseling: Some practical problems and issues. *JR Soc Med* 1987;80:278-280.

⁷ Marzuk PM, Tierney H, Tardiff, K, et al: Increased risk of suicide in persons with AIDS. *JAMA* 1988;259:1333-1337.

⁸ Rinaldi RC: *HIV blood test counseling: AMA physician guidelines*. Chicago, IL, American Medical Association, 1988.

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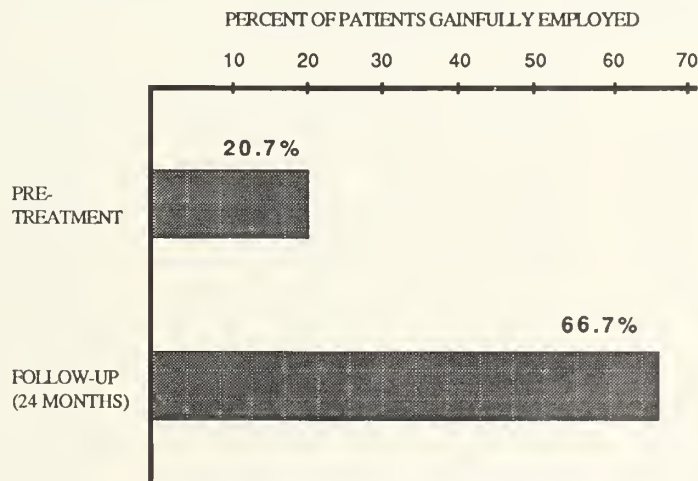
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References

1. *USP DI Update*, September/October 1988, p 120
2. *Br J Clin Pharmacol* 1985;20:710-713
3. Data on file, Lilly Research Laboratories
4. *Scand J Gastroenterol* 1987;22(suppl 136):61-70
5. *Am J Gastroenterol* 1989;84:769-774

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Drug Interactions—No interactions have been observed with theophylline, chloridiazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect, but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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Additional information available to the profession on request.



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AIDS and Hospice Care of Rhode Island

Henry C. McDuff, MD, Jr
Mary Eleanor Toms, MD
Judy Gordon, RN
David Rehm, MSW

AIDS patients now represent over 7% of our current caseload and HCRI has given comprehensive nursing and medical care for 14% of all persons who have died of AIDS in Rhode Island.

Hospice Care of Rhode Island (HCRI), like many hospice programs around the country, first encountered the reality of the AIDS epidemic in 1985. Until then, HCRI had devoted itself exclusively to the care of terminally ill

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cancer patients and, as awareness of the hospice option grew, had been struggling to meet the growing, daily demand for its services. Nevertheless, in 1985 HCRI joined a then small number of hospice programs who moved toward serving persons with AIDS. At that time the HCRI Board approved an alteration in our mission statement which allowed us to include noncancer patients as space became available in the program. We then undertook a series of intramural training efforts to educate as well as sensitize our staff and volunteers to the serious issues, some unique, in providing care for persons with AIDS. Having thus made these preparations, we admitted our first patient with AIDS on January 8, 1986, learning quickly that to provide the level of care needed by these patients would entail an even more intense and personal level of education for our staff and volunteers.

In retrospect, our initial decision to admit and care for these patients was both ambivalent and

naive. The first referrals were slow in coming, and eventually our agency was forced to inspect again our established policies and objectives. In the ensuing two years, HCRI adjusted its guidelines and program goals to reflect the realities of caring for AIDS patients. The first major change was to abolish our admissions criterion that life expectancy be six months or less. Predicting life expectancy for AIDS patients is both difficult and demonstrably unreliable. Further, in contrast to our philosophic premise of providing only palliative care for cancer patients, we now began to offer more aggressive treatment regimens which were clearly appropriate for persons with AIDS. Finally, as an agency, we undertook to become a full and active partner in the developing Rhode Island care-network for persons with AIDS. As

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

HCRI: Hospice Care of Rhode Island

a result of these revised agency policies and a more realistic commitment, there has been a steady increase in the number of AIDS patients served by HCRI. AIDS patients now represent over 7% of our current caseload and HCRI has given comprehensive nursing and medical care for 14% of all persons who have died of AIDS in Rhode Island.

Our first AIDS patient was a 41-year-old male with multiple and aggressive opportunistic infections. He survived 75 days and died of Pneumocystis pneumonia. Since early 1986, HCRI has admitted 24 patients with confirmed AIDS. Sixteen of these patients have since died, 10 at home and 6 in the hospital. Length of stay in Hospice Care has varied from as little as 3 days to as long as 240 days. The demographic and medical profile of our 24 patients, including identified risk factors, differs inappreciably from the much larger, published series of AIDS cases in the United States. The great majority of our patients are male (23 of 24), their ages ranging from a one-year-old infant to a 53-year-old man. The encountered opportunistic organisms include: Pneumocystis carinii, Candida albicans, Toxoplasma gondii, avian Mycobacterium infection, and cytomegalovirus. Cases of Kaposi's sarcoma, lymphoma and pancytopenia have also been identified.

Our experience to date has convinced us that hospice services are both helpful, appropriate and cost-effective in the terminal care of persons with AIDS. The common misconception of hospice as an agency focussed narrowly on death rather than on the enhancement of the quality of life has been an especially frustrating barrier in reaching this population. Understandably, AIDS patients, who are primarily quite

young, find such an association unsettling and many, therefore, do not take advantage of our services. Another area of concern is the fact that only 9 of the 179 AIDS patients discharged from our regional hospitals in 1988 were referred for subsequent home-care. This statistic is troubling for two reasons: First, that these patients were deprived of considerable support, assistance and case management potentially available to them through hospice; and second, that their inpatient stay might have been shortened if a coordinated home-care followup had been offered.

Our experience to date has convinced us that hospice services are helpful, appropriate and cost effective in the terminal care of persons with AIDS.

The role of the hospice physician in treating AIDS is no different than in the management of other diseases for which there is no cure. The medical care of humans with AIDS is customarily complex; and toward the end of life, two major issues remain which require continuing attention — the control of pain and the alleviation of confusion. The control of pain should be no different than in other circumstances. The fear of generating addiction through the use of opiates has been shown to be baseless. The correct titration of oral morphine should proceed in the same manner as with pain of other causes, the goal being to prevent breakthrough pain.

Anxiety, depression and dementia may increase the underlying pain. And the attending physician may be so involved in the immediate medical issues that it becomes the place of the palliative care physician to work with

the patient on the problems of pain, depression and confusion, fulfilling, in a promise made by all physicians: "To cure sometimes; to comfort always."

Further information may be obtained by calling the Hospice Care of Rhode Island central office (401) 272-4900.

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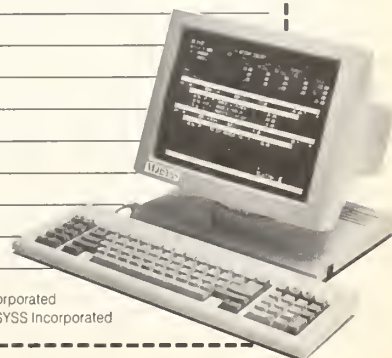
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Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

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Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

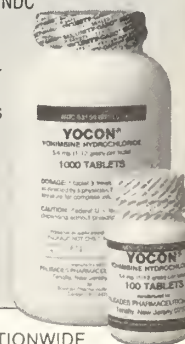
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon[®] 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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AIDS in Africa: A Personal Perspective

Seth Berkley, MD

... cases of a wasting illness with a high mortality and of unknown etiology, but clearly a new disease, appeared in some villages of Central Africa.

The first cases of the Acquired Immunodeficiency Syndrome (AIDS) were recognized in homosexual men in San Francisco in 1981.¹ Soon thereafter cases were identified in other parts of the United States and Europe in homosexual men and in intravenous drug users.² The etiology of the illness was unknown until isolation of the causative agent in late 1984.

During this same time period, cases of a wasting illness with a high mortality and of unknown etiology, but clearly a new disease, appeared in some villages of Central Africa. Physicians accustomed to examining the oral cavity as part of their normal physical examination noted the association of oro-pharyngeal candidiasis, a condition they had never seen before in adults, with this wasting syndrome. It was only with development of a serologic test for the Human Immunodeficiency Virus (HIV-1) in 1985 that this illness in Africa was con-

firmed to be caused by the same agent as AIDS in the United States.

In 1986, a new virus, HIV-2 — genetically related but distinct from HIV-1 was isolated from a patient from West Africa with an AIDS-like illness.³ Much less is known about the biology of this agent, its distribution or the resultant illness. It causes a similar clinical illness to HIV-1 but the course of infection seems to be less fulminant. It is primarily seen in West Africa and currently is less common than HIV-1 infection. For these reasons, this paper will confine its discussion to the epidemiology of HIV-1.

Prior to the availability of the serologic test for HIV-1 public health workers were only able to monitor clinical cases of AIDS, the end-stage of HIV infection. The advent of serologic testing now permitted the direct monitoring of the growing epidemic of HIV infection. Early studies done in Africa with the initial generation of HIV test procedures were fraught with problems of cross-reactivity. This led to wildly high and unreliable estimates of infection. Over time, improved test reagents have significantly reduced this problem. Recent studies with highly specific tests have, nevertheless, demonstrated the dramatic magnitude of the HIV epidemic in sub-Saharan Africa. This

paper will attempt to provide a broad perspective on the epidemic of HIV in Africa today.

Diagnosis of AIDS

Differences in the presentation of the disease (see below) as well as the unavailability of sophisticated diagnostic facilities have made use of the standard CDC/WHO Case Definition for AIDS problematic. As a result, the World Health Organization convened a meeting in Bangui, Central African Republic, in 1985 to develop a simple clinical case definition for use in Africa.⁴ This clinical definition requires no laboratory or pathologic testing to establish the diagnosis. The definition is primarily used for surveillance and reporting of disease and is moderately specific for HIV-1 infection but is not sen-

ABBREVIATIONS USED:

AIDS: Acquired Immune Deficiency Syndrome

CDC: Centers for Disease Control

HIV: Human Immunodeficiency Virus

PCP: *Pneumocystis carinii* pneumonia

STD: Sexually transmitted diseases

WHO: World Health Organization

Seth Berkley, MD, a graduate of Brown University's medical school, is currently on the health science staff of the Rockefeller Foundation. He has recently returned from Africa where, for over two years, he was the epidemiologist for the Uganda Ministry of Health.

sitive.* The definition has been subsequently modified in certain countries to increase its usefulness. In Uganda, a modified definition (table 1) had a specificity for HIV-1 infection of 92% and a sensitivity of 52%.⁵ As a result of the imperfection of the definition, the diagnosis of AIDS in a specific patient, must be individually assessed by the health care worker and is determined by multiple factors including the criteria of the clinical definition.

The clinical diagnosis of pediatric cases of AIDS in Africa presents even greater problems. A similar clinical case definition for pediatric cases had a sensitivity of 35% and a specificity of 87%.⁶ Modifications of the definition have not led to substantial improvement. Even inclusion of HIV serologic testing, which is not available in most areas in Africa, does not solve the diagnostic difficulties since infants of infected mothers may carry passively transferred maternal antibodies against HIV for months after birth without infection. New tests to define pediatric HIV infection are desperately needed.**

AIDS Surveillance

Routine disease reporting systems in most African countries are extremely limited. Case reporting for AIDS is also a politically sensitive issue.*** Despite these problems, AIDS cases have been reported in 48 (92%) of the 52 African countries. In some countries, like Uganda, attempts are made to report all patients with HIV illness. In others, like Zimbabwe, stringent criteria for diagnosis means that AIDS cases are

* For this definition, sensitivity is the probability of identifying HIV infection using the clinical definition, specificity is a measure of the probability of not meeting the definition when infection is not present. Since many persons are asymptomatic with infection, the sensitivity of a clinical diagnosis for identifying HIV infection will always be low.

Table 1

AIDS in an adult in Uganda is defined by the existence of at least 2 of the major signs associated with at least 1 minor sign, in the absence of known causes of immunosuppression such as cancer or severe malnutrition or other recognized etiologies.

1. Major signs:
 - a) weight loss \geq 10% of body weight;
 - b) chronic diarrhea $>$ 1 month;
 - c) prolonged fever $>$ 1 month (intermittent or constant).
2. Minor signs:
 - a) persistent cough for $>$ 1 month without tuberculosis;
 - b) generalized pruritic dermatitis;
 - c) herpes zoster;
 - d) oro-pharyngeal candidiasis;
 - e) chronic progressive or disseminated herpes simplex infection;
 - f) generalized lymphadenopathy;

The presence of generalized Kaposi's sarcoma or cryptococcal meningitis are sufficient by themselves for the diagnosis of AIDS.

under-reported. Health care facilities in many African countries are inadequate and largely confined to the urban areas. The dearth of such facilities in rural areas reduces further the accuracy of reporting. Finally, the lack of a standardized and accepted case definition for AIDS/HIV disease makes comparison of case rates and prevalences among the different countries difficult.

As of 1 February 1990, 40,519 cases of AIDS have been reported to WHO from the African continent. Under-reporting of cases is a common occurrence; it is estimated that there have been about 350,000 cumulative cases in Africa (10% reporting of the cases).

** Polymerase Chain Reaction (PCR) and HIV antigen tests hold promise in improving the diagnosis in infants. However, at the moment neither will be of sufficient simplicity or inexpensive enough to be considered for use in a clinical setting in Africa.

This compares with an estimated 62% of cases reported in the Americas and 78% in Europe. Despite these problems in reporting, available data from a number of sources confirms a high prevalence of HIV infection in the center of the continent including the nations of Kenya, Tanzania, Uganda, Zambia, Zimbabwe, Malawi, Rwanda, Burundi, Zaire, Congo and the Central African Republic (figure 1). Conversely, there are nearby areas of Africa with lower prevalence of HIV infection. Nigeria with almost one-fifth of the sub-Saharan population has remained relatively free of HIV infections.

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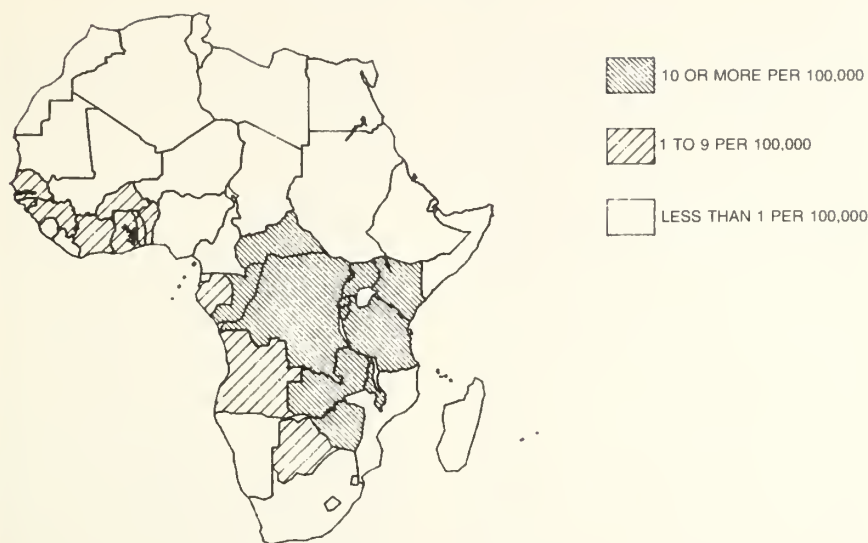
The Illness in Africa

Although the HIV isolated from African patients is phenotypically similar to virus isolates from AIDS patients in the United States and Europe, the resultant presentation of AIDS is quite different. Clinical disease in AIDS is mostly a manifestation of the underlying opportunistic infections. The most common presentation for AIDS in the United States is pulmonary disease. Opportunistic infections are most commonly

*** For example, the country of Zaire, which has one of the most extensive AIDS research programs with large documented cohorts of AIDS cases, reported no AIDS cases to the World Health Organization from June 1987 to November 1989. During the same period, hundreds of cases from Zaire were reported in the medical literature. They recently began reporting cases again.

Figure 1

REPORTED AIDS CASES IN AFRICA
FEBRUARY 1, 1990



Pneumocystis carinii pneumonia (PCP), tuberculous and non-tuberculous mycobacterial infections and Kaposi's sarcoma. In contrast, African patients tend to present with a wasting disease associated with chronic gastrointestinal involvement (locally known as slim disease) and dermatologic involvement. In Uganda, 82% of the cases presented with weight loss and 60% with diarrhea.⁷ Tuberculosis and salmonellosis are common superimposed infections. Herpes-zoster, a common disease in developed countries in persons not HIV-infected was almost unknown in general practice in Africa prior to the appearance of HIV. It has appeared in an epidemic fashion with very high specificity, approaching 100% for HIV infection.* PCP is rare and non-tuberculous mycobacterial infection almost unreported in Africa. Neurologic manifestations, such as dementia and psychoses, which are felt to be direct mani-

festations of neurologic infection with HIV are seen in both areas.

African patients (with AIDS) tend to present with a wasting disease associated with chronic gastrointestinal involvement (locally known as slim disease) and dermatologic involvement.

The regional variability in clinical presentation of AIDS probably represents differences in patient's exposure to environmental pathogens as well as differences in nutritional status. Missed diagnoses may also play some role since sophisticated diagnostic facilities are often not available in many African countries. Nevertheless, when studies of African AIDS patients, using state-of-the-art technology, are carefully performed these differences in presentation have been confirmed.

The HIV epidemic is becoming a major challenge to physicians (and other health care workers) in Africa where they are encountering HIV infection combined with numerous acute infectious

and parasitic diseases. It is becoming commonplace for health care workers to question HIV infection in any atypical presentation of a disease. In some hospital wards in cities in central Africa, 50% or more of the in-patients are HIV infected. This means that physicians and other health workers have had to learn new diagnostic and therapeutic skills without the benefit of continuing medical education and relevant medical literature.

In the developed world the mean interval from HIV infection to the onset of AIDS is felt to be about 10 years (ie, approximately 50% of HIV infected persons will develop AIDS in 10 years). Although data from Africa are not complete, the length of time from the onset of HIV infection to the development of AIDS is probably shorter and the time from onset of AIDS to death is dramatically reduced. Most AIDS patients in Africa will die with their first opportunistic infection.

Transmission

Africa is an ethnically and geographically heterogeneous continent with over 50 countries. This paper will confine itself to heterosexual (type II [see below]) transmission in sub-Saharan Africa since it is the most important of the transmission methods on the continent. However, we should not forget that all three patterns (as described by WHO⁸) of HIV transmission have been described on the continent: Pattern I (primarily homosexual and bisexual males and intravenous drug users) in South Africa; Pattern II (primarily heterosexual) in sub-Saharan Africa; and Pattern III (newly introduced HIV infection from travellers and visitors but not yet spread to the general population) in North Africa.

Only three routes of HIV transmission have been successfully

* In Uganda, herpes-zoster is locally called "belt disease" due to the dermatomal distribution. The significance of its appearance, even in a healthy person is rapidly becoming known and dreaded.

defined: from (1) blood and blood by-products, (2) mother to child and (3) sexual activity.

Although data from Africa are not complete, the length of time from onset of HIV infection to the development of AIDS is probably shorter and the time from onset of AIDS to death is dramatically reduced.

1. Blood and blood by-products: Prior to the development of blood screening in 1985, a relatively large percentage of HIV infections were transmitted by contaminated blood and blood by-products. As an example, it was estimated that 516 HIV-seropositive blood transfusions were given annually to children with malaria in but one pediatric hospital in Zaire.⁹ Blood screening has now virtually eliminated this risk in developed countries. In contrast, in Africa, transmission by contaminated blood transfusion still occurs in some areas despite heroic attempts by the Red Cross and the WHO's Global Program on AIDS to bring blood screening to as many transfusion centers as possible. However, transmission by blood now only represents a small percentage of instances of HIV transmission. This is particularly true since sophisticated health facilities are the first to receive HIV screening equipment and they do the bulk of the transfusions. Fortunately, less well equipped rural health units that are less likely to have functioning HIV screening are also less likely to give blood transfusions.

Initial claims of extensive HIV transmission from blood contaminated instruments used for traditional scarification have not been substantiated. Use of non-sterilized needles and syringes

may be responsible for some HIV transmission but this does not currently seem to be a major route.

2. Mother to child: Infection may be transmitted from the infected mother to the infant in utero, during delivery or in the neonatal period. Initial estimates of a mother-to-child HIV transmission rate of 50% have now been reduced to 25-30%. Factors such as the clinical stage of maternal HIV infection may be an important factor determining transmission. Although a few well-documented cases of HIV transmission by breast milk have been documented in the developed world, the attributable risk of this route is unknown. Since increased childhood mortality is known to occur when breast milk is withheld, all international authorities have continued to strongly recommend breast feeding in Africa, even when the mother is HIV infected.

3. Sexual route: In the initial cases in developed countries the primary route of transmission was sexual, primarily between male homosexuals and was particularly linked in individuals having receptive anal intercourse. In fact, there had been doubts expressed as to whether the infection could be transmitted by vaginal intercourse from females to males. With increasing knowledge, it is quite clear that bidirectional heterosexual transmission can occur in developed countries even after only one sexual encounter.

In Africa, bidirectional heterosexual transmission was demonstrated early in the epidemic. Homosexual relations and intravenous drug use are less common in sub-Saharan Africa and therefore do not contribute substantially to transmission. Heterosexual anal intercourse in many African countries is also reported to be uncommon and is not sus-

pected to play a major role in transmission.

Models of HIV Spread in Africa

Although the epidemiology of HIV transmission is complex, three waves of spread may be hypothesized in sub-Saharan Africa.*

(1) Initially, a small number of female prostitutes became infected. In many areas of Africa prostitutes, especially low-priced ones with a very large number of partners, have developed very high infection rates. In Nairobi, Kenya, the infection rate was documented to rise from no infections in 1981 to greater than 90% of the prostitutes infected in 1987. Similar patterns are seen in other sub-Saharan countries. Serosurveys in these areas during this period of the epidemic would show seropositivity only in prostitutes and certain other high risk groups such as prostitute-clients as seen in STD Clinics.

(2) Over time, these prostitutes infect a large number of male sexual partners. Males with money to spend on prostitutes, such as business persons or truck drivers are the first to acquire infection thus explaining the early occupation-specific differences in infection rates. High numbers of male sexual contacts with these prostitutes result in a predominance of HIV infection in males. This is currently postulated to be the pattern in Abidjan, Ivory Coast where the sex ratio of AIDS cases in the hospital is 4.8 males to 1 female.¹⁰

(3) These infected males go home to their villages and towns and infect their stable and casual female sexual partners resulting in large numbers of seropositive persons in the general public. At

* This is obviously an oversimplification of a very complicated issue. In fact in most countries all three waves are occurring simultaneously in different areas and even sometimes in the same community.

this point the concept of targeting "high-risk" persons for control efforts becomes meaningless. All persons in non-monogamous relationships in the population must be seen as potentially infected. During this phase, gender infection rates are close to equal or with a slight predominance of infection in females. This appears to be the case in Uganda where the sex ratio of infected persons is approximately 1.4 females to every male.

Ease of Heterosexual Transmission

Studies in developed countries have suggested that heterosexual HIV transmission is a relatively inefficient route of infection. It is estimated, for example, that the risk of transmission in the United States during a single unprotected heterosexual encounter with an infected partner is 1:500.¹² HIV transmission from male to female has been felt to be more efficient than transmission from female to male.¹³

... researchers have the impression that the efficiency of HIV transmission in sub-Saharan African heterosexuals is higher than that determined in Europe and the United States.

Although comparable data are not yet available from Africa, researchers have the impression that the efficiency of HIV transmission in sub-Saharan African heterosexuals is higher than that determined in Europe and the United States. The reason for this difference has yet to be adequately explained. Viral strains have not been shown to be of different virulence and there has not been any convincing evidence of a genetic difference in susceptibility to HIV. The presence of certain risk factors (described as co-

factors by some authors) have been postulated to increase the efficiency of transmission by facilitating the transfer of viable virus during coitus. This can be a result of an increased susceptibility to infection with the virus and/or an increased infectiousness of a person. These factors include male non-circumcision, STDs (particularly genital ulcerative diseases), an immune system chronically stimulated by chronic parasitic and infectious burdens, and use of oral contraceptives in females. However, a recent and disturbing report from Belgium raises questions as to the necessity of these co-factors for high efficiency transmission.¹⁴ The paper describes a cluster of HIV infections transmitted from a single African male where 11 (56%) of 18 women having sexual contact became infected, two after having only one sexual contact with the patient.

The Demographic Impact of HIV Infection

The first documented evidence of HIV infection in Africa is from a 1959 serologic specimen from Zaire in which HIV antibodies were detected.¹⁵ The earliest virus isolate was obtained from a specimen stored in 1976, also from Zaire.¹⁶ This suggests that the virus has been circulating, to some degree, in Africa for at least a few decades.

Initial reports of an exclusive urban location for HIV infection have been misleading. National and sentinel serologic surveys have shown high rates of HIV infection throughout many sub-Saharan countries particularly in the countries described above. Although urban infection rates are substantially higher than rural rates, the predominant rural location of the population means that the disease is important in both areas. For example in

Uganda it is estimated that 80% of the HIV infected persons live in the rural areas despite an infection rate in the cities which is twice as high.¹⁷ This pattern is not seen in all areas. In a small rural isolated community in Zaire, the seroprevalence for HIV remained steady at 0.8% over a 10 year period from 1976-1986.¹⁸ This suggested that a traditional village life carries a low risk of infection. However, by 1986, prostitutes in the area had a seroprevalence of 11% suggesting that the seroprevalence would probably begin soon to rise.

The first documented evidence of HIV infection in Africa is from a 1959 serologic specimen from Zaire in which HIV antibodies were detected.

Infection rates in certain groups such as prostitutes, STD patients and truck drivers tend to be much higher than the general population, but in most countries in central sub-Saharan Africa the concept of HIV infection restricted to such high-risk groups is no longer valid. Infection rates in the general population are 1.3% to 17.8% in rural and urban Rwanda¹⁹ and 2.7% to 14.5% in rural to urban Uganda.¹⁷ Limited serologic surveys in subgroups in other countries in the region suggest infection rates may be similar, but data from these other countries must be considered as yet inadequate for a representative comparison.

Information on the speed of spread of the epidemic is also limited. In Uganda, in one missionary antenatal clinic in Kampala, the capital city, infection rates have increased dramatically. Regular random sampling of clinic attendees have shown infection rates to increase from 10.6% (1985), 13.6% (1986) to 24.1% (1987).²⁰

There is a biphasic age distribution of HIV infection. There is a small peak in the 0-4 year old group then almost no infection in children 5-12 years of age. Infection rates tend to peak in adults of reproductive age. In Uganda, the peak age of HIV infection for females is 20-24 years versus 25-29 years for males.¹¹ A similar age-specific distribution is seen in other central African countries. This means that the bulk of AIDS morbidity and mortality will occur in the most economically productive age group. At a time when these countries are struggling to improve their economies, AIDS will have a profoundly negative effect on development.²¹

The higher infection rate in women and the earlier age-specific peak of female infection has implications for families and their social structure. There will be a substantial number of HIV-infected infants born in the next few years. Most of these will die of HIV-related disease in the first few years of life. Furthermore, even in those children born to an infected mother who are fortunate enough to remain uninfected, we can expect an increase in childhood mortality because of the illness of the infant's traditional caretaker, its mother. With infection rates in childbearing age women as high as 20-25% in some African cities, this epidemic has the potential to reverse the great gains made in reducing childhood mortality by the GOBI* child survival revolution.

There will be yet other effects on the nuclear family. With HIV/AIDS, unlike some other causes of parental mortality, when one parent is infected there is a high likelihood that the other is simi-

larly infected. In polygamous societies, all members of the nuclear family may be infected. This means that the number of children with both parents dying will be increasing. Traditionally, orphans are cared for by the extended family, but with the high burden of AIDS in some areas, how will families care for the large number of orphans? In Rakai, a particularly affected district in Southeastern Uganda, there are estimated to be over 23,000 HIV-related orphans out of a population of 165,000 children below 15 years of age.¹⁷

In Rakai, a particularly affected district in Southeastern Uganda, there are estimated to be over 23,000 HIV-related orphans out of a population of 165,000 children below 15 years of age.

The World Health Organization estimates that of the approximately 6 million persons currently infected with HIV, more than 3,000,000 live in Africa and that there have been 350,000 cases of AIDS. Therefore, at the present time, more than half of all HIV-infected persons are living in sub-Saharan Africa. Even more alarming is the estimate that over 75% of the world's HIV-infected females live in sub-Saharan Africa. Women are extremely important in most African societies, performing a large part of the agricultural work as well as the raising of their children. The numbers of HIV-infected women who will become ill with AIDS and die over the next decade will profoundly change some African societies.

In developed countries, rates of transmission in non-intravenous drug-using homosexual males have dramatically de-

creased and transmission via blood products has virtually ceased. Rates, unfortunately, continue to rise in intravenous drug users. However, as the number of drug users represents but a small fraction of the population, the rate of new infections in the developed world is decreasing while rates in the developing world are increasing. With the burden of disease shifting towards Africa there is the danger that HIV/AIDS will begin to be seen as another "tropical disease" in the future with the resulting loss in attention and research activity.

Can we be optimistic? Even in countries most severely affected by the AIDS epidemic such as Uganda, it is estimated that 94% of the general population remains uninfected.¹⁷ With 50% of the population under 15 years of age in many African countries, there is a new uninfected cohort entering the sexually active age group each year. This group must be protected. Africans with the assistance of international agencies and voluntary organizations are diligently working to slow and stop the transmission of the virus. These immense efforts must be undertaken within the framework of an overworked, overburdened and under-compensated health care team and infrastructure. There is also an opportunity here. Using the worldwide interest and funds generated by the international community for AIDS, we can mobilize resources and infrastructure not only for AIDS, but towards the general improvement of health for the population.

Sexuality in African culture is poorly understood. With health education as our only effective weapon at this point, new and innovative methods to change sexual behaviour are desperately needed. These must be developed, tested and widely disseminated.

* GOBI is an acronym for growth monitoring, oral rehydration for diarrhea, breast feeding and immunization — programs that have been at the heart of the movement for international child survival.

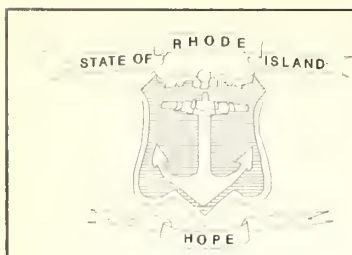
inated until a vaccine or effective and practical therapy can be found. In the meantime, African health care workers and policy makers will be required to deal with treatment issues for the half or more of the three million HIV-infected persons who will become AIDS cases during the next decade.

With the burden of disease shifting towards Africa there is the danger that HIV/AIDS will begin to be seen as another "tropical disease" in the future with the resulting loss in attention and research activity.



References

- ¹ Pneumocystis pneumonia — Los Angeles. MMWR 1981;30:250-2.
- ² Update on Kaposi's Sarcoma and opportunistic infections in previously healthy persons — United States. MMWR 1982;31:294-301.
- ³ Clavel F, Guetard D, Brun-Vezinet F, et al. Isolation of a new human retrovirus from West African patients with AIDS. Science 1986;223:343-346.
- ⁴ World Health Organization Workshop on AIDS in Central Africa. Bangui, Central African Republic, Oct 22-24, 1985.
- ⁵ Widy-wirski R, Berkley SF, Downing R, Okware S, Recine U, Mugerwa R, Lwegaba A, Sempala S. Evaluation of the WHO clinical case definition for AIDS in Uganda. JAMA 1988;260:3286-3289.
- ⁶ Colebunders RI, Greenberg A, Nguyen-Dinh P, Francis H, Kabote N, Izaley L, Davachi F, Quinn TC, Piot P. Rapid communication evaluation of a clinical case definition of AIDS in African children. AIDS 1987;1:151-153.
- ⁷ Berkley SF, Okware S, Naamara W. Surveillance for AIDS in Uganda. AIDS 1989;3:79-85.
- ⁸ Mann JM, Chin J. AIDS: A Global Perspective. N Engl J Med 1988;319:302-303.
- ⁹ Greenberg AE, Nguyen-Dinh P, Mann JM, Kabote N, Colebunders R, Francis H, Quinn TC, Baudoux P, Lyamba B, Davachi F, Roberts JM, Kabeya N, Curran JW, Campbell CC. The association between malaria, blood transfusions, and HIV seropositivity in a pediatric population in Kinshasa, Zaire. JAMA 1988;259:545-549.
- ¹⁰ DeCock KM, Odehouri K, Moreau J, Kouadio JC, Porter A, Barrere B, Diaby L, Heyward WL. Rapid emergence of AIDS in Abidjan, Ivory Coast. Lancet 1989;408:411.
- ¹¹ Berkley SF, Naamara W, Okware S, Downing RG, Konde-Lule J. The Epidemiology of AIDS and HIV infection in women in Uganda. Abstract 12 in the Abstract Volume of the IV International Conference on AIDS and Associated Cancers in Africa. 18-20 October 1989, Marseille, France.
- ¹² Hearst N, Hulley SB. Preventing the heterosexual spread of AIDS. Are we giving our patients the best advice? JAMA 1988;259:16, 2428-2432.
- ¹³ Friedland GH, Klein RS. Transmission of the human immunodeficiency virus. New Engl J Med 1987;317:1125-1134.
- ¹⁴ Clumeck N, Taelman H, Hermans P, Piot P, Schoumcher M, DeWit S. A cluster of HIV infections among heterosexual people without apparent risk factors. The New Engl J Med 1989;321:1460-1462.
- ¹⁵ Nahmias AJ, Weiss J, Yao X, Lee F, Kodsi R, Schanfield M, et al. Evidence for Human Infection with an HTLVIII/LAV like virus in Central Africa, 1959. Lancet 1986;i:1279-80.
- ¹⁶ Getchell JP, Hicks DR, Svinivasan A, Health JL, York DA, Malonga M, Forthal DN, Mann JM, McCormick JB. Human Immunodeficiency Virus isolated from a serum sample collected in 1976 in Central Africa. J Infect Dis 1987;156:833-837.
- ¹⁷ Vivian Asedri. 790, 522 Ugandas are HIV positive. The New Vision, vol. 4 no. 271, December 1, 1989, Kampala, Uganda.
- ¹⁸ Nzilambi N, DeCock KM, Forthal DN, Francis H, Ryder RW, Malebe I, Getchell J, Laga M, Piot P, McCormick JB. The prevalence of infection with human immunodeficiency virus over a 10-year period in rural Zaire. N Engl J Med 1988;318:276-9.
- ¹⁹ Rwandan HIV Seroprevalence Study Group. Nationwide community-based serologic study of HIV-1 and other human retrovirus infections in a central African country. Lancet 1989;i:941-943.
- ²⁰ Carswell JW, Lloyd G. Rise in prevalence of HIV antibodies recorded at an antenatal booking clinic in Kampala, Uganda. AIDS 1987;1:192-3.
- ²¹ Gillespie S. Potential Impact of AIDS on Farming systems. Land Use Policy 1989;October:301-312.



HEALTH BY NUMBERS

Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

AIDS/HIV Surveillance

The Rhode Island Department of Health (RIDH) designated AIDS as a reportable disease in 1983. Seven cases were reported in that year with 5 new cases of AIDS diagnosed in 1984, 13 in 1985, 37 in 1986, 75 in 1987, 85 in 1988, 86 in 1989, and 27 reported cases as of April 30, 1990.

Males dominate (84%) among reported cases in Rhode Island; however, the percentage of female cases (16%) is significantly higher than the national figure (9%). Despite representing less than 7% of the total population in Rhode Island, the proportion of AIDS cases in Blacks and Hispanics has remained substantial and relatively constant (31% 1987; 33% 1988; 33% 1989; 30% 1990).

An analysis of selected transmission categories by year shows a slight increase in the categories of Homosexual IV Drug User and Heterosexual Contact in 1989, while the percentages of cases in Homosexual/Bisexual Males and Heterosexual IV Drug Users have experienced a slight decrease (Table 1).

Counseling and Testing Site Activity

As of August 1, 1989, state law mandated HIV antibody testing of prisoners, prostitutes, and persons convicted of possession of IV drug use equipment. It also required that physicians and other health care providers offer testing to women seeking prenatal care

Table 1: RHODE ISLAND AIDS CASES BY
SELECTED TRANSMISSION CATEGORIES; BY YEAR
1983-1989

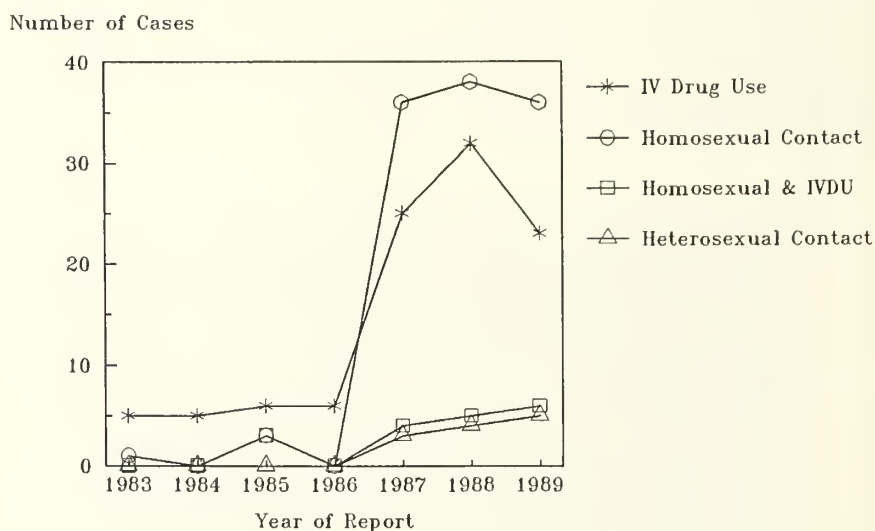


Table 2: RHODE ISLAND HIV TESTING DATA
August 1, 1989 through April 30, 1990

Test Site Categories	Number Tested	Number (%) Positive
Anonymous*	1,065	26 (2.4)
Routine**	4,301	50 (1.2)
Mandatory (Prison)	4,530	213 (4.7)
Private MDs/Labs	4,019	25 (0.6)
Other***	4,808	118 (2.5)
TOTAL	18,723	432 (2.3)

*Includes: Department of Health sites at Cannon Building in Providence and Benjamin Rush Building in Cranston.

**Includes: Health Centers, Hospital Clinics, Drug Treatment Centers, and STD Clinics.

***Includes: Colleges, Inpatient Hospital Tests, and Free-Standing Clinics.

or family planning services, to persons suspected of having a sexually transmitted disease, persons involved in a service offered at a facility for IV drug users, and marriage license applicants. The reporting of positive HIV test results by unique client code to the RIDH was also required by this legislation. This program became effective on September 1, 1989 and compliance to date exceeds 70%. The routine testing sites, which include agencies under contract with the RIDH, as well as private settings, are in compliance (Table 2).

HIV Seropositivity

Of the 330 reported cases to date of HIV infection in Rhode Island, 253 (77%) were males and 77 (23%) were females. Ninety-five Blacks, 63 Hispanics and 2 Asians represent 48% (160/330) of the total cases. No known cases of HIV infection have been reported in Native Americans (Table 3). The principal behavior associated with transmission of the virus is IV Drug Use (51%), followed by Homosexual Contact (14%) and Heterosexual Contact (13%). There have been no reported cases of HIV infection in persons with Hemophilia or other related coagulation disorders (Table 4).

Table 3: RHODE ISLAND HIV INFECTION:
RACE & SEX;
September 1, 1989 - April 30, 1990
N = 330

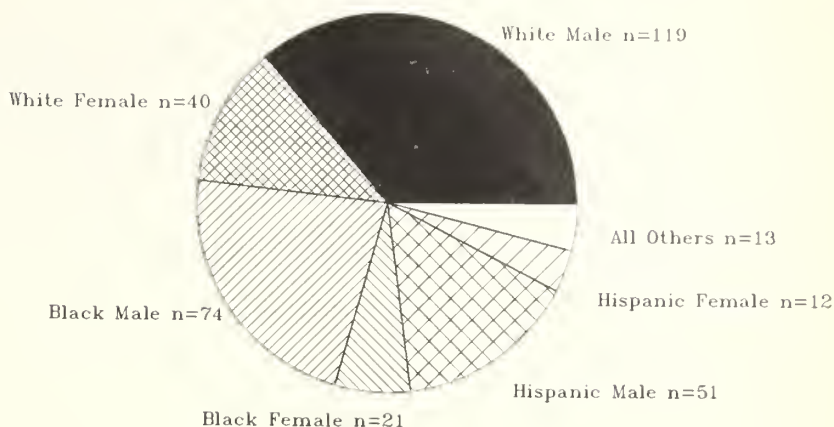
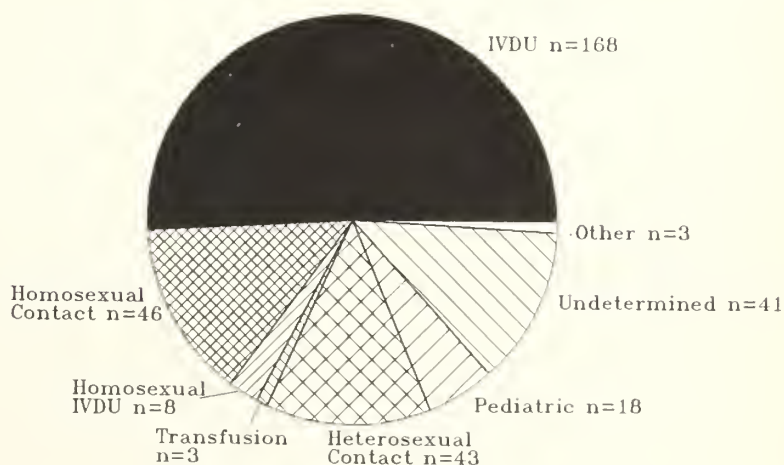


Table 4: RHODE ISLAND HIV INFECTION:
RISK CATEGORY;
September 1, 1989 - April 30, 1990
N = 330



Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with March 1990	
	March 1990 Number	Number	Rates
Live Births	1,377	15,689	15.8*
Deaths	845	9,679	9.7*
Infant deaths	(9)	(153)	9.8†
Neonatal deaths	(6)	(125)	8.0†
Marriages	382	8,343	8.4*
Divorces	379	3,780	3.8*
Induced Terminations	700	7,994	509.5†
Spontaneous Fetal Deaths	81	1,082	69.0†
Under 20 weeks' gestation	(79)	(977)	62.3†
20+ weeks' gestation	(2)	(96)	6.1†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with December 1989		
	December 1989 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	346	3,447	347.1	4,431.5
Malignant Neoplasms	230	2,452	246.9	6,647.0
Cerebrovascular Diseases	56	592	59.6	882.0
Injuries (Accident, Suicide, Homicide)	32	439	44.2	10,058.0
COPD	32	317	31.9	450.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (July, 1940)

The lead article, entitled "Medical Service and the National Health Program," is written by Dr W. G. Phippen, President of the Massachusetts Medical Society. The author reviews the Social Security Act of 1935, its provisions for maternal and child welfare and the outcome of subsequent federal legislative action pertaining to health insurance. In answer to "... an undercurrent of criticism of and antagonism to the American Medical Association," he outlines the steps taken and the beliefs expressed by "organized medicine" in response to this criticism. Amongst these beliefs, he lists:

They believe that any system of prepayment sickness insurance should allow the insured free choice of physicians.

They accept the idea of prepayment hospitalization insurance such as we know as the "Blue Cross" in Massachusetts.

They have no quarrel with the expenditure of government funds for grants in aid to states for public health, child welfare and maternity services, provided they are under local control.

They have no objection to federal funds for hospital construction, provided all available beds are first used and a need for more

is shown, and provided that private as well as public hospitals are aided.

They believe that the care of the indigent is a public charge. They believe that this care varies in different states and that it should be considered a local problem, and that the granting of federal funds should be based upon such local needs.

Drs C. A. McDonald and M. Korb publish the case report of a 36-year-old woman with a right post-frontal astrocytoma, verified by surgical intervention. Despite the previously published observations by others "finding slow waves in cases of cerebral tumors" the electroencephalogram in this case was non-contributory.

Drs R. G. Murphy and E. Damarjian describe "a case of riboflavin deficiency with idiopathic hypochromic anemia, presenting typical skin lesions, with bilateral transverse fissures on a greasy, scaly base at the angles of the mouth, extending toward the cheek, and dry scaly desquamation of the lower lip. The satisfactory response to treatment with synthetic riboflavin and characteristic remission of the idiopathic hypochromic anemia has been shown."

This issue of the *Journal* summarizes the proceedings of the 1940 Annual Meeting of the Medical Society chaired by its president, Dr Lucius C. Kingman. The reports of the various Society committees are offered, including the report of the Committee on Nominations. (Note: Of the many physicians proposed for the various standing committees, only the name of Dr J. P. Eddy, 3rd, is still on the roster of the Society.) The evening ended with, "... an excellent dinner at the Pomham club. . . . The speaker of the evening, The Reverend Roberts A. Seilhamer described a visit to Helsinki, 'The World's Most Northerly Capital.' "

In his annual report, the Secretary of the Society notes that the physician membership in May, 1939 was 484; that 30 members were lost through deaths or resignations, and 32 added, resulting in a current membership of 486.

A report from Rhode Island Hospital lists the following new interns: Drs Linus A. Sheehan, Malcolm S. Allan, William A. Reid, James H. Crowley and Emil J. Koenig, Jr. All five, coincidentally, are graduates of Tufts Medical College.

Four recent texts are reviewed

in this issue of the *Journal*. One of these books, by W. E. Davis, describes the author's medical practice in the Belgian Congo. "In one year," summarizes the reviewer, "65,000 patients came to his clinic. In the same year he did 536 major operations. He did not encounter cancer, appendicitis, gall-bladder disease or typhoid fever."

* * *

Twenty-Five Years Ago (July, 1965)

The lead article by Dr C. L. Dunham, Director of the Division of Biology and Medicine, US Atomic Energy Commission, is entitled, "Atomic Energy — Its Present Day Status in Medicine." The article discusses recent developments in metabolism using radioactive tracers for the study of such physiologic phenomena as blood flow, cardiac output, liver function, albumin synthesis, and the turnover rates of various metallic ions in the body; it also outlines scanning techniques of the brain and other organs, using a substance called Technetium-99m. The author talks about advances in the use of tracer materials which may be "on the verge of clinical application." For example, the use of immunologic techniques to localize radionuclides in specific tissues, or the attempts to produce radio-active antibodies to specific neural neoplasms. The author further describes neutron activation analysis for the identification of trace substances. In considering whole body radiation injury (ed. note: This written over two decades before the tragedy of Chernobyl), he reviews the various pathologic reactions including the cessation of bone marrow function, and speculates, "Bone marrow transplants can now be accomplished in rodents; but it is not certain that they would be life-

saving or even desirable in humans except in the case which had enough radiation to destroy essentially all of the marrow permanently."

M. B. Wilbur, E. E. Healy and E. R. Tighe discuss the nursing needs and resources of Rhode Island, based upon a state-wide survey of nurses. During the early months of 1964, 5,564 professional nurses were registered by the Division of Professional Regulation of the Rhode Island Department of Health. Of these 1,156 neither lived nor worked in Rhode Island. Of the remaining 4,408, the following characteristics are summarized by the authors: Only 38 are male; of the 4,370 female nurses, 67.5% are married, 8.2% widowed or divorced and 24.3% single. At the time of the survey, 74.8% are employed in nursing. The recorded sites of nursing employment include: hospitals (69.9%), private duty (10.1%), public health (6.1%), school or industrial nursing (5.9%), office nursing and other sites (8.0%). The article concludes by making a number of strong recommendations which, by one means or another, are designed to increase the number and enrollments of nursing schools within Rhode Island and to use more wisely and prudently the skills of those already in the nursing profession.

In another page of this issue of the *Journal*, it is noted that there are 284,271 physicians in the United States as of Dec. 31, 1964. Licensing board examination failures in 1964 total 1,181. Failure rates for US medical school graduates, 1.7%; for Canadian medical school graduates, 7.8%; for graduates of schools of osteopathy, 9.4%; and for foreign-trained physicians, 31.8%.

A paper by M. Silverman, I. J. Laszlo, and J. Cramer, describes the development of a diagnostic and treatment program for de-

viant pre-school children employing the facilities of a children's neuropsychiatric hospital (Bradley Hospital) and a rehabilitation center for neurologically impaired youngsters (Meeting Street School). The article notes the immense problems in aiding severely disturbed children, the role of the parents in the therapeutic process, and the modest results achieved.

R. M. Young, the microbiologist at the Rhode Island Hospital, describes new and promising approaches to immunologic diagnosis through the use of fluorescent dyes attached to antibodies. The author describes how the laboratory identification of certain bacterial, fungal, parasitic and even viral agents may be facilitated by such techniques.

The lead editorial commends Mt. Sinai Hospital of New York on the imminent opening of its medical school. The editorial states, "It will be the first new medical school in the United States since before World War I to be sponsored by a hospital without University affiliation." The editorial concludes, this being 1965, "It (Mt. Sinai Medical School) presents a striking contrast to another interesting project in medical education, that of Brown University, which is oriented first to basic science, with clinical proliferations only indefinitely perceived at some future time. It will be fascinating to compare the progress and future development of these two interesting experiments."

Further editorials talk (1) of the need for a convention center in Rhode Island, (2) the miraculous flight of the Gemini astronauts in space and, in the same year, the dreadful carnage on the American highways with 48,000 deaths and 3,840,000 injuries, and (3) the increasing hazards of truck and bus exhaust.

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UNDERSTANDING CME

Edited by
Kimberly Allyn,
RIMS CME Coordinator

Janice Miller, M.Ed.,
Director,
Office of CME
Brown University

ESSENTIAL #3 — OBJECTIVES

The sponsor shall have explicit objectives for each CME activity. The sponsor shall:

- 1) State the educational need(s) which the individual activity addresses.**
- 2) Indicate the physicians for whom the activity is designed.**
- 3) List any special background requirements of the prospective participants.**
- 4) Highlight the instructional content and/or expected learning outcomes in terms of knowledge, skill, and/or attitudes.**
- 5) Make these objectives known to prospective participants.**

Objectives are a key step in helping the planning committee develop the most effective educational format and in publicizing and evaluating the CME program. Therefore, the objective should be written before deciding on the educational format. Well stated objectives help clarify the communication process with the planning committee, the program faculty and the target audience.

Objectives communicate to the selected faculty the specific needs of the target audience. Objectives

inform prospective participants what they can expect to learn while attending the program and whether the program is relevant to their needs or interests. Referring to the objective when completing an evaluation determines whether the program addressed what it planned.

Educational objectives may be broken down into three areas:¹

1. *Learner* objectives reflect what the student should know or be able to do at the end of a learning period.

2. *Instructional* objectives reflect what the instructor intends to accomplish.

3. *Behavioral* objectives reflect what the learner might be expected to do differently (behavior change) as a result of what has been learned.

When writing objectives it is important to use specific action verbs. This helps clarify what the learner is expected to accomplish. Avoid words that are vague and general. Of course, the exact choice of words will depend on the material being presented. Example:

The participant will be able to identify the psycho-social factors important in the development of the child abuse syndrome.

ESSENTIAL #4 — PLANNING AND DESIGN

The sponsor shall design and implement educational activities consistent in content and method with the stated objectives. The sponsor shall:

1) **Design and implement educational activities responsive to the characteristics of prospective participants, such as, knowledge levels, professional experience, and preferred learning styles.**

2) **Document use of systematic planning procedures.**

3) **Make educational content and methods known to prospective participants.**

The teaching format of the program should be planned after the objectives have been developed as these indicate what format would be most suitable. For example, an objective concerned with learning CPR would not be accomplished with only a lecture format.

The planning committee should look at three areas when designing the program:

a) *What will be the most effective format to ensure participants acquire the intended knowledge?*

Though the lecture-slide format is chosen most often, a va-

riety of learning approaches can be explored, depending on the objective. Discussion groups and simulations are just some of the possibilities.

b) Who is the most knowledgeable speaker to present the information?

The ideal choice for a speaker is someone who is an expert in that area and has the ability to relate to an audience.

c) What facilities and equipment are necessary to obtain a successful presentation?

The facility should be well lit, acoustically adequate, and comfortable with opportunity for speaker-audience interaction.

Other important considerations for the arrangement of a successful program are: date and time, place (accessibility), space (potential number of partici-

pants), format, audio-visual equipment requested by speaker (make sure all equipment is working correctly), attendance (a system for physician sign-in and distribution of evaluation sheets), notification and publicity, transportation (if needed by speaker), and budget (based on program specifics and available resources).

Documentation is a vital part of any CME program. Written records of committee/planning group meetings, faculty correspondence, and facility or financial arrangements is useful information for evaluating the overall program, maintaining continuity, and future planning. In addition, as part of the accreditation requirement, program planning records designated as Category 1 must be kept for four years.

References

¹ Rosof, A. Stating Objectives. Continuing Medical Education: A Primer. Edited by A. Rosof & W. Felch. Praeger Publishers 1986; Chapter 4:32.

Coming up:

Essential #5 and #6

Questions are encouraged and should be addressed to:

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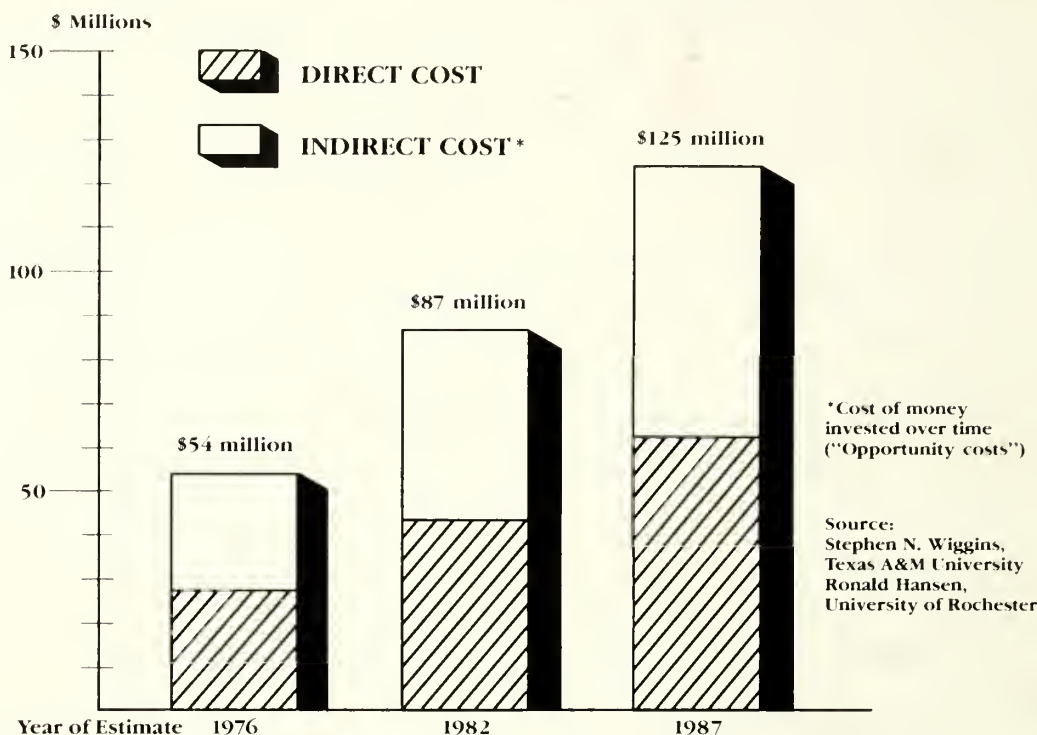
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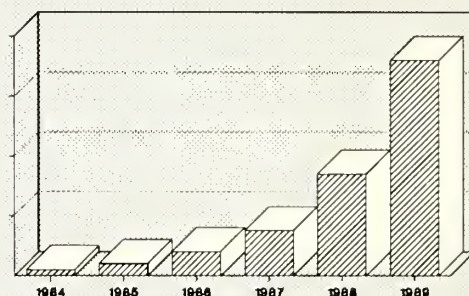


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EDITORIALS

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On Making Mistakes

There is one certain conclusion to be reached by watching someone fall through a manhole — namely, avoid manholes. When watching others, from a distance, struggle through their daily lives, it is a relatively simple matter to distinguish right from wrong, to see the proper path to take, to be certain in one's judgment. Mistakes are so easy to identify, so self-evident, when observed from the isolated comfort of *Journal* pages or retrospective reports. Rarely, however, do these reports convey the real atmosphere of confusing and contending circumstance, the conflicting urgencies and travail as well as the problems which both color the fabric of a physician's working consciousness and provide the substrate for rare lapses in otherwise good judgment. It is nevertheless essential that physicians seek out their mistakes, study them and, in an imperfect world, devise mechanisms to lessen them.

This issue of the *Journal* is devoted, for the most part, to assessments of 4 brief case histories each with notable ethical problems and, perhaps, mistakes in judgment by physicians. The *Rhode Island Medical Journal* has adopted a policy of presenting to its readers the various and often divergent views of the State's professional leadership in matters of medical ethics and policy. In order to

achieve this aim, the *Journal* periodically publishes problem cases followed by the earnest commentaries of selected physicians, clergy and other professionals from the Rhode Island community. Typically, these problem cases are fraught with moral ambiguity and offer no simple, ethical solution. In this issue, the views of 10 physicians, 3 clergy and 2 educators are summarized.

The first case embodies the painful recollection of a Pawtucket physician when during his clerkship in another state he observed a serious lapse in medical care followed by an equally serious lapse in judgment by his professional superiors. We are provided with a skeletal outline of the pertinent clinical events. This is followed by a thoughtful and assertive commentary by Professor Ed Beiser. Important questions are asked — and then answered without compromise or equivocation. To provide the readers with a still wider perspective, the *Journal* asked 4 prior presidents of the Rhode Island Medical Society and the current Chief Administrative Officer of the RI Board of Medical Licensure and Discipline to offer their personal views on this case. These bluntly realistic commentaries by Drs Coustan, Mathieu, Rakatansky, Sullivan and Hamolsky, agree on one tenet: That medicine adhere to those high standards to which

it professes, and then to support actively the newly established system designed to hear and investigate all complaints of unprofessional conduct (from whatever source), to determine whether there is any merit to the charges, and finally to recommend sanctions if the charges are substantiated.

The continued workings of the Board of Medical Licensure and Discipline, and its uncompromising support by the leadership of the Rhode Island Medical Society is truly a tribute to the strength and integrity of the medical profession in this state: Zealous enough to seek out professional mistakes; compassionate enough to protect confidentiality until judgment is reached; and assertive enough to support whatever sanctions are decreed.

The Editorial Board of the *Journal* believes that it is the *Journal's* proper role to raise and discuss disquieting issues. A broad representation of views will be solicited. And inevitably both agreement and disagreement will arise. If the ethical problems of medicine could but be reduced to some numeric scale of judgment, then medicine will have retreated to the status of a trade: a highly sophisticated and learned trade, but nonetheless a trade. By accepting, struggling with and defining our views concerning problems of moral dimension, we confirm ourselves as mem-

bers of a learned profession.

Future issues of the *Journal* will occasionally address problems such as the 4 which may be found in these pages; and accompanying commentaries will be supplied by a widening number of experienced physicians practicing in this state.

"Experience is a wonderful thing," Mark Twain supposedly remarked, "it permits you to recognize a mistake when you make it again." Medicine doesn't permit such casualness. Physicians are certainly not perfect. But if they are incapable of learning from their mistakes, the profession now has assured means that such mistakes will not be repeated

Stanley M. Aronson, MD

Mistakes (Benign Variety)

Mistakes come in all shapes, sizes and denominations. In medicine, mistakes are unlikely sources of humor; and by definition they are deserving only of deliberate and searching discussion. But in one corner of the stern business of medicine there remains some latitude for laughter, some gentle appreciation of our personal foibles. The *Journal* receives a moderate, and increasing, number of scientific contributions for publication. These offerings are serious efforts by our colleagues, representing much labor in designing the work, studying the writings of others, assembling data and then translating all of this to a tightly coherent, logical and persuasive manuscript. A mistake or two may sometimes go undetected by the author; which allows the editors of this *Journal* to zealously collect such slips of the

word-processor — and if sufficiently delightful, to publish them at periodic intervals. The most recent ones, without attribution, are printed below:

"... the patient had slowed, irregular aspirations."

"... examinations of the GI track."

"... and in two cases, sex was not available."

"... the high cost of impatient care."

"... in the gross appearance of the sessile, villainous adenoma ..."

Stanley M. Aronson, MD
Kimberly J. Allyn

Another Look at the New State Medicare Law

The original version of this article appeared in the Rhode Island Medical News, December 1989. It is reprinted here at the request of the Board of Medical Licensure and Discipline, which notes that there continues to be uncertainty and confusion about the new state Medicare law, in effect since January 1, 1990.

While only about 7% of Medicare claims for physician services in Rhode Island ever involved any balance billing, that small percentage presumably dropped to zero after December 31, 1989. The reason for the drop is a new state law that prohibits balance billing of all Medicare beneficiaries, regardless of their age or financial means.

It is important for physicians and patients alike to understand what the term "balance billing" means. To give an example: If a physician's normal

charge for a service is \$75 and Medicare's so-called "reasonable" or "allowable" fee is \$50, Medicare will pay \$40 and the patient is responsible for \$10. Under the new state law, the physician may not "balance bill" for any part of the remaining \$25 that would constitute his or her normal fee.

Putting it another way, "balance billing" means charging a patient more than 100% of Medicare's "reasonable" or "allowable" fee; 80% of that fee comes from Medicare, and 20% of it, as well as the annual deductible, comes from the patient. While balance billing is prohibited in Rhode Island as of January 1, 1990, there is no prohibition on charging the 20% copayment and the annual deductible to the patient; indeed, federal Medicare requires physicians to collect copayments and deductibles routinely from Medicare patients.

A physician who does "balance bill" a Medicare patient after December 31, 1989, may be found guilty of "unprofessional conduct" and therefore subject to sanction by the Board of Medical Licensure and Discipline. Unlike a similar measure in Massachusetts, the Rhode Island law is not directly tied to licensure.

In particular, the new statute states that "A physician, who, if he or she agrees to treat a beneficiary of health insurance under title XVIII of the Social Security Act, charges or collects from such beneficiary any amount in excess of the reasonable charge for that service as determined by the United States secretary of health and human services" shall be guilty of "unprofessional conduct."

What follows below represents the Society's best judgment of how the law might

reasonably be understood and what physicians should do and avoid doing in order to comply:

1. **Does the new state Medicare law require me to see Medicare patients?** No.
2. **Does it require me to sign a participation agreement with Medicare?** No.
3. **Does it require me to accept assignment?** No. You may still bill the patient directly, rather than Medicare, as long as you do not bill for more than 100% of Medicare's "allowed" or "reasonable" fee (80% of which is reimbursed by Medicare, and 20% of which is paid by the patient or the patient's supplemental insurance). Physicians should note, however, that starting Sept 1, 1990, even unassigned claims must be processed and submitted by the physician, who may not charge for this clerical service; this change is a federal mandate.
4. **What does it mean that the new state law prohibits "balance billing" of Medicare beneficiaries?** The term "balance billing" means billing for more than 100% of Medicare's "allowed" or "reasonable" fee, 20% of which is the patient's responsibility and 80% of which is reimbursed by Medicare. For example, if your regular fee for a certain service is \$175, but Medicare's "allowable" or "reasonable" fee is \$100, then \$100 is all you may charge or collect: \$80 will come from Medicare and \$20 will come from the patient or the patient's supplemental insurance. The new state law prohibits you from sending the patient a "balance bill" for all or part of the remaining \$75 of your regular fee.
5. **Should I collect the 20% copayments and annual deductibles from the patient?** Yes. Doing so does not constitute "balance billing." The 20% is included in Medicare's "allowable" or "reasonable" charge. Moreover, federal Medicare requires physicians to collect those amounts routinely from Medicare patients.
6. **What about my MAACs (Maximum Actual Allowable Charges) under Medicare?** MAACs, which are federally imposed limits on balance-billing, became irrelevant in Rhode Island on January 1, because all balance-billing is now prohibited.
7. **How can I be sure that I am in compliance with the state's new Medicare law?** It is difficult to be sure in all cases. On occasions when you, as a non-participating physician, elect to collect from a Medicare patient without yourself submitting a claim to Medicare, you must be careful neither to charge nor collect more from the patient than 100% of Medicare's "allowed" or "reasonable" fee (80% of which the patient can recover from Medicare). Assuming in addition that the intent of the new law is to limit out-of-pocket expenses for Medicare patients, it seems reasonable to assume that you may bill for your customary charge in some instances, particularly: **a)** whenever you take Medicare assignment, and **b)** if you "participate" in Medicare and thus always take assignment. (Taking assignment means you submit the claim to the Medicare carrier, which is Blue Cross/Blue Shield of Rhode Island, receive 80% of Medicare's "allowable" or "reasonable" charge from that carrier, and collect the remaining 20% from the patient or from the patient's supplemental insurance, assuming the patient has already met the annual deductible.)
8. **If I do not take assignment, how do I know what Medicare's "allowed" or "reasonable" fee is for a given service?** The "allowed" or "reasonable" fee is defined as the lowest of these three: the "prevailing" fee locally, your own "customary" fee, or your actual charge. The local Medicare carrier, Blue Cross/Blue Shield of Rhode Island, notifies physicians annually of the prevailing and customary fees for the various services performed in each practice. The carrier last sent notice of prevailing fees and customary fees to physicians in March 1990. If you lack current information for your practice, you may request it from the Medicare office of Blue Cross/Blue Shield of Rhode Island. As a practical alternative, you may wish to instruct your office staff to keep a record of payments you receive from Medicare in instances where you do take assignment, then use that information as a guide when you elect not to take assignment.

9. **If I do not take assignment and bill only for 100% of Medicare's "allowable" or "reasonable" fee, how do I maintain my Medicare profile?** You cannot; your profile will stagnate. For practical purposes, however, your profile of "customary" charges will almost always be higher than the out-dated "prevailing" charges anyhow; therefore (since Medicare's "allowed" or "reasonable" fee is defined as the lowest of the prevailing, customary, or actual charges) your profile of customary charges is likely to be irrelevant to your actual reimbursement. (Moreover, as the RBRVS is phased in beginning in 1992, personal pro-

files will be phased out. In addition, beginning September 1, 1990, physicians will be required to perform the paper work even on unsigned Medicare claims without being able to charge for that service; thus that remaining advantage of nonparticipation in Medicare will disappear.)

10. **Will my Medicare profile affect my Blue Shield profile?** No. The two are separate.
11. **What if I bill for services that are not covered by Medicare?** Services for which Medicare has not developed "prevailing," "customary," or "allowed" fees are outside the Medicare system; since the new

state law refers specifically to Medicare's "reasonable" (= "allowable") fee, it would appear safe to assume that the law is inapplicable to services that are not covered by Medicare, such as cosmetic plastic surgery.

Newell E. Warde, PhD
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References

1. *USP DI Update*, September/October 1988, p 120.
2. *Br J Clin Pharmacol* 1985;20:710-713.
3. Data on file, Lilly Research Laboratories.
4. *Scand J Gastroenterol* 1987;22(suppl 136):61-70.
5. *Am J Gastroenterol* 1989;84:769-774.



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Indications and Usage: 1. *Active duodenal ulcer*—for up to eight weeks of treatment. Most patients heal within four weeks.

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3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

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Carcinogenesis, Mutagenesis, Impairment of Fertility: A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

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an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect, but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

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Hepatic: Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L). The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular: In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS: Rare cases of reversible mental confusion have been reported. **Endocrine:** Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic: Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental: Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity: As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other: Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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HARD CHOICES: Medical Ethics, Law and Health Policy

Reporting Physicians' Mistakes

Edward N. Beiser, PhD, JD

A practicing physician in Rhode Island recalls the following case which took place when he was a fourth-year medical student clerking at a busy teaching hospital in another state. The physician, who prefers to remain anonymous, continues to be troubled by the experience. Because of the importance of the issues it raises, he is willing to share the case for discussion by his colleagues.

Case Presentation: The patient was a 58-year-old, employed male who came to the emergency room of a university hospital. His wife stated that he had been increasingly confused over the last few days. He seemed "not quite himself," lethargic, forgetful, not recognizing familiar people, and neglectful of his personal hygiene. She stated further that he was a smoker, occasionally used alcohol, had no significant medical problems and was taking no medication. She was not aware of any history of trauma, signs of infection, vomiting, headache or visual changes in her husband.

A complete physical examination by the medical student revealed a disheveled, lethargic male in no

distress. He did not cooperate in or resist physical examination, was oriented to person only, and was able to answer simple questions in a monotone. Vital signs were normal as was the general physical examination. No focal neurologic signs were found and no papilledema was noted. Laboratory tests, including serum alcohol, serum ammonia, electrolytes, and arterial blood gases were in the normal range.

The patient was assigned to the neurology service. A CT scan of the head was ordered and obtained within 2 hours of admission and the intern went to radiology to have the scan interpreted. The patient's CT scan was read as normal by the resident physician in radiology and the intern then reported this finding to the neurology team. A lumbar puncture was then performed showing a grossly elevated opening pressure. The patient was now increasingly unresponsive with slowed, irregular respirations. And despite vigorous attempts, the patient lapsed into an irreversible coma and died several days later.

Upon reviewing the patient's CT scan on a later occasion, it was found that the intern had brought the wrong films to the radiology resident for interpretation. The actual CT showed a large, left frontoparietal mass, consistent with subdural hematoma, causing significant shift of the midline. The patient's family was told by the senior resident physician of the team, however, that "the patient's condition had deteriorated because of the seriousness of his disease." At

no time during the patient's hospital stay or after his death did any physician indicate to the family that a mistake had been made.

Discussion

What is a physician properly to do when he either observes or discovers evidence of a significant error by another physician in the treatment of a patient, where that error resulted in real harm to the patient, and where the physician who made the mistake declines to inform the patient (or the patient's family), whether by outright lying or by failing to call relevant information to the patient's, or family's, attention? To put this complex question more directly: What should a physician do when he discovers that a fellow physician is covering up a mistake which hurt a patient?

The case presented above is distinctive in a number of respects which serve to differentiate it from other situations involving mistakes.

First, there is no doubt that a mistake was made. The wrong CT films were read. Apparently the hospital was extremely busy and there were 2 patients on the same service with the same family name. The intern produced "Peter Smith's" film, so to speak, when his patient was really "Paul Smith." The

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term, "mistake," is sometimes applied to the situation in which a judgment call proved, after the fact, to be wrong. Failure to order a test, failure to recognize a sign or symptom, failure to treat aggressively, may result from poor practice. But such situations will sometimes result from honest differences in professional judgment. Physicians who know all too well that every maloccurrence can unfairly be labeled malpractice, may be reluctant to make judgments about "mistakes." Here, however, the existence of a mistake is beyond dispute — the wrong film was read. But even where matters of judgment are involved, certainly there are situations in which an intellectually honest physician will conclude that a colleague's action (or inaction) was beyond the pale of reasonable practice, and deserves to be called a "mistake."

Second, there is no doubt that the patient's death was hastened by the mistake. Had this patient's CT scan been read properly, the lumbar puncture would never have been undertaken. He died because the team, in this setting, did not know that the lumbar puncture was contraindicated. The case is all the more troublesome because had the correct CT scan been read, it is likely that the subdural hematoma could have been evacuated. Medicine had something good to offer this patient. Instead, because of a mistake, a diagnostic procedure was undertaken which hastened his death. Consider, by way of contrast, a case discussed at a teaching conference, some years ago, at a Brown-affiliated hospital. Because the wrong EKG strip was read in the emergency room, a patient with seri-

ous heart disease was discharged. This time the patient and the doctors were lucky. The patient was admitted by her private physician several days later, apparently none the worse for the delay. Should that patient have been told? Should her family have been told? Should the administration of the hospital or of the relevant residency training program have been told?

Why Report Mistakes? To Whom to Report Mistakes? Most basic is the need to report mistakes to the one who made them. How can physicians grow, how can they perfect their methods, if they are unaware of what they have done? That this is obvious does not make it easy in practice. Certainly physicians, and others in positions of authority, have a strong obligation to inform those that they supervise of their mistakes. Thus, in the case presented, the senior resident physician or the chief of the service were obliged to inform the intern.

Physicians in private practice sometimes become aware of errors committed by physicians for whose work they bear no particular supervisory responsibility. It may be a doctor in another state (the easiest case to complain about). It may be another doctor with privileges in your hospital. It may be a doctor funded by the insurance program that you participate in.

One doesn't make friends by calling the shortcomings of others to their attention. One doesn't enhance business, and increase referrals, by calling the shortcomings of others to their attention. But certainly, with due deference to differences in medical judgment, one contributes to the quality of care, and to the standards of the profes-

sion, if one sensitively informs another physician of evidence of a mistake. The physician who wishes to improve the quality of care offered to his or her patients will at least in some sense welcome information about his or her own errors.

Mistakes can also be reported to persons in positions of authority. This is perhaps most obvious in a formal training setting such as a residency program. Hospitals employ a variety of mechanisms to maintain quality control. And of course there are boards of licensure and discipline, boards which are widely thought to exercise very weak supervision over the profession. The logic of reporting someone else's error to such a board or governing body is to permit the determination of whether a particular mistake is part of a systematic pattern requiring remediation. Is the physician impaired? Is his technic substandard? Or is he, perhaps, working under unacceptable conditions? Were the interns in the university hospital involved in this case-report so overworked that it was to be expected that they might well grab the wrong CT film? Was there a problem in the way that the hospital kept its records, or labeled its films? Such issues can only be addressed if mistakes are reported.

Rhode Island physicians will be acutely aware of a much publicized case involving a physician who went to prison for installing pacemakers in patients who did not require them. Public outcry against the "conspiracy of silence," and the assertion that doctors "covered up" for each other, led to legislation creating the Board of Medical Licensure and Discipline. The statute requires that certain events be reported to

the Board — such as limitations on physicians' privileges, or malpractice claims. The statute further authorizes complaints about unprofessional behavior. My reading of the statute is that physicians (and others) are permitted to report unprofessional conduct; they are not legally obliged to do so. If they do file a complaint in good faith, the statute seeks to immunize them from liability or retaliation.

The statute creating the Rhode Island Board of Medical Licensure and Discipline went into effect on January 1, 1987. Since then, fewer than 5 complaints have been filed by physicians alleging non-professional conduct by other physicians. The reading of the wrong CT scan in the case reported above (which, I repeat, took place in another state) was clearly "unprofessional conduct" within the meaning of the Rhode Island statute. Moreover, the outright lie told by the senior resident physician to the family would, in and of itself, appear to be unprofessional conduct within the meaning of the Rhode Island statute. (The definition of unprofessional conduct includes the willful filing and making of false reports in the practice of medicine.) If the Board of Medical Licensure and Discipline is to play a meaningful role in the assurance of quality care in Rhode Island, then a case such as this one most certainly ought to have been reported. To say this, to be sure, says nothing about what action the Board might properly have taken.

If an unambiguous error (reading the wrong film) with an unambiguous result (a contra-indicated diagnostic procedure was performed, death ultimately resulting) is not reported to a board of licensure, if an outright lie to the deceased

patient's family is not reported to the board, then the general public is entitled to have no confidence in the board's ability to regulate the standards of medical practice. A question which remains open in Rhode Island is whether physicians should be required, as distinct from being permitted, to file complaints about the unprofessional conduct of others.

When to Tell the Patient or the Family. The fourth-year medical student, confronted with what he conceived to be a cover-up of blatant malpractice, went to see the chief of the service in which he was training. He was essentially told to remain silent. "We have learned all we can from this case; nothing good will come of upsetting the family." I find this reaction extremely unsatisfactory for at least 4 reasons:

First, from a totally pragmatic point of view, such a cover-up may well buy trouble in the years ahead. Professionals in the field of risk-management report that one way to minimize losses is to admit mistakes and offer credible compensation. Families who discover later that they have been lied to, and juries who smell a cover-up, are likely to react in a punitive way.

Second, and most importantly, the patient's family is legitimately entitled to compensation. Perhaps the intern, the hospital and the training program can learn nothing more from this case. But a 58-year-old breadwinner has died. His family's legitimate entitlements are hardly offset by the embarrassment to the intern and the hospital.

Third, the patronizing attitude that doctors know best what patients and their families are entitled to be told is no

longer acceptable in the practice of ethical medicine. A family is entitled to know the true cause of death. A patient is entitled to know the true cause of prolonged pain or suffering. Patient autonomy, respect for the patient as a competent adult, requires that he be told the truth, even if his doctor feels uncomfortable in imparting this truth.

And fourth, I am troubled by the message being sent to the intern by his chief's decision to lie to the family. No one is perfect. Doctors will make mistakes — good doctors, caring doctors. And sometimes those mistakes will have grave consequences. The decision to lie about the mistake in no way helps the intern come to grips with what he has done. Perhaps it even encourages him to accept an unrealistic view of doctor as Superman.

Conclusion

This case was presented by a physician because, years later, he still worried about whether he had done the right thing. I told him that his initial response was correct. He had gone through channels and had consulted with the chief of the service. Having done this, and having received no satisfaction, ought he have gone further? Certainly it seems inappropriate to hold a medical student to a higher standard than that which his superiors — the senior resident and the chief of service — were abiding by.

My conclusion is that the response of this unnamed university teaching hospital was significantly deficient. This mistake ought not to have been swept under the rug; both the family and public authorities ought to have been notified. This would have permitted

compensation to the patient's family, and would have permitted professional evaluation both of the conduct of the intern, and the conduct of the hospital.

It is difficult to imagine that parallel cases do not occur in Rhode Island from time to time. It is the hope of the physician

who reported this case, and the author of this discussion, that readers of the *Journal* will consider their own reactions. Would you report such an incident? Would you want to be required to report such an incident? Do physicians, as members of an honorable profession, have a particular obli-

gation to help to ensure the quality of medical care received by the general public?

Commentaries on Reporting Physicians' Mistakes

Donald R. Coustan, MD

I am in total agreement with Dr Beiser that the medical student in the case in question performed appropriately, and that the response of the chief of service was deficient. Our ethical standards as physicians require that we tell the truth to our patients, and I believe that includes the families of patients who have died. If physicians cannot be relied upon to be truthful, then we cannot expect the trust that is absolutely essential to the practice of medicine. In the case in question, the fact that the wrong CT scan was analyzed was withheld from the

family, and that is reprehensible. An appropriate way for the chief of service to have handled the situation would have been to ask the family to confer about the results of the autopsy once available (as is done routinely at our hospital, and I suspect many others), and to inform them of the problem at that time.

Dr Beiser asks, "Do physicians, as members of an honorable profession, have a particular obligation to help to ensure the quality of medical care received by the general public?" Of course we do. The case in point does not seem to be a difficult ethical question, since it hinges on the concealment of facts. However, there is a much broader issue to be considered. It has been my experience that such obvious cases of patients suffering major disasters as a result of gross mistakes are rare, and it is rarer still for the facts not to be obvious

to the patient or the family. What is much more common is an adverse outcome in which there is disagreement about the actions of a particular physician, whether before or after the fact. If I, as a medical student, house officer, or perhaps a colleague, disagree with the care given by another physician, do I have an obligation to tell that patient or that family about my concerns? I think that this is a distinctly different

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ABBREVIATIONS USED:

AMA: American Medical Association

CT: Computerized tomography

DO: Doctor of Osteopathy

EKG: Electrocardiogram

HMO: Health Maintenance Organization

PRO: Professional Review Organization

RIMS: Rhode Island Medical Society

question from the preceding one.

Physicians fulfill their obligation to help ensure the quality of medical care received by the public, in many ways every day. Adverse outcomes are routinely reviewed by quality assurance committees in every hospital of our state. The Rhode Island Medical Society has committees which are designed to protect the public as well as to help physicians cope with problems of alcohol and drug dependence or competence. The State Board of Medical Licensure and Discipline was created to protect the public from unprofessional conduct by physicians. Any physician, even a medical student, who questions the conduct of another physician may go to any of these sources and ask for an investigation. Hospitals have credentialing committees. Although our system isn't perfect by any means, I don't think that any other profession is constantly under the scrutiny that is experienced by practicing physicians in the 90s.

I don't believe that a medical student, house officer or colleague should go directly to a patient or family to report a disagreement with the responsible physician's management of their care. When I worked as an orderly and nurse's aide, before medical school, I heard the nurses second-guessing the house staff and attendings frequently. When I was a medical student and house officer I found myself second-guessing my superiors with some regularity. This kind of criticism is part of growing up in medicine, but an important part of the maturing process is learning not to make snap judgments based upon incomplete information. Things often seem to be obvi-

ous when one's knowledge base is limited. If we think one of our colleagues has performed inappropriately in a particular case, we ought to go to the chief of service or the appropriate quality assurance committee and ask that the case be reviewed, so that all of the facts can be available. If poor care was given, the particular physician should be made aware of the finding and suggestions should be made for improvement.

"Although our system isn't perfect by any means, I don't think that any other profession is constantly under the scrutiny that is experienced by practicing physicians in the 90s."

It is my view that differences in judgment are much more common than is the sequestration of facts from patients. While our responsibility for truth telling dictates that facts not be hidden, and that medical records must be accurate. I do not believe that society is well served if a medical student, house officer or attending physician feels compelled to inform the patient of another physician, or their family when they disagree with the judgments or actions of that other physician.

Facts must not be withheld from a patient or family. Facts and opinion are not the same thing. The medical profession best fulfills its obligation to the public by supporting strong quality assurance mechanisms, and by viewing hospital quality assurance as a method for helping physicians provide the best possible care by informing them when they are not doing so.

Peter L. Mathieu, Jr. MD

There are many problems in the protocol as presented to us by Professor Beiser. The unnamed physician has been struggling with what he conceives to be his implicit guilt by way of a decision made years ago. There were many errors of judgment and the former medical student has tempered his guilt by focusing on the errors of his superiors.

The medical student examination noticed no papilledema, an unlikely situation in view of the very high spinal fluid pressure. While the protocol focuses on the misreading of the CT scan (because they had the wrong patient's films), it misses the problem that no adequate medical examination seems to have been made. A "doctor's" examination, given the patient's history, would have included asking him to stand with his eyes closed. His poor balance would have led the way to the proper diagnosis through subsequent neurological mapping. Testing and technology exist to confirm or disprove a diagnosis, not as a substitute for the professional interaction of physician and patient. Thus the department chief failed in his most significant duty of physician responsibility to the patient and

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proper supervision of the physicians entrusted to his teaching program.

Technology itself is neither good nor evil. Things like CT scans do all we tell them, but our human resources and our technologies should be directed to protecting and caring for the patient: A "mission impossible" that is truly person-oriented and less case-directed. Each health care worker must have a meaningful and self-perceived role in the patient's need. Administrators need to be in the hospital actively overseeing and auditing for mistakes. The relationship between ethics, human nature, progress, and practice must be addressed.

The family's loss is much more important than the embarrassment of the hospital staff. The Chief of the Department sent a very poor signal, "don't talk about it," to the medical student, intern, and to the family. People in authority were basically false witnesses in this instance.

Somewhere along the line, I learned that a man acts well according to reason. St. Thomas Aquinas, disciple of Aristotle, who was pupil of Socrates, said a well disciplined soul required guidelines. I embrace Plato's cardinal virtues for human contact of temperance, justice, prudence, and compassion. Had these been applied to the present case, the actions taken would have been different.

If we place the "mistake" in a more social context, it becomes clear that somehow silence has become oddly moral when a wrong has been done. It does not make sense. A person of good will will strive to clarify, and to apply certain guidelines by which responsible action in the face of wrong done is made

clear. Judgment and wisdom are based on common principles and character of the judge. Jacques Maritain believed in judgment by inclination and not by reason. I believe the family has a right to know — as it happened. Who made the mistake? Who was in charge and what is the name of the physician(s) that reports to the patient? He should identify himself so that the doctor-patient relationship of which we all speak so fondly operates in a human form.

"While the protocol focuses on the misreading of the CT scan (because they had the wrong patient's film) it misses the problem that no adequate medical examination seems to have been made."

Of the rich broth of our social-ethnic life together, in the ways it seasons us all without our knowing it, we know very little. Is this a fair charge? I don't know. Physicians should rectify mistakes. Should they report mistakes? To whom? I recommend since we are called a health care team, that we pursue direct knowledge of what goes on in each other's environments. We might encourage patients to meet members of the team face to face.

In the article no doctor seems to be in charge. No line of responsibility to the patient is evident. Internal mission statements shared with the patient might highlight the human support he needs. If my analysis is correct, the physician will give more careful thought when he comes across a mistake. Think strategically rather than theo-

retically. Think more about what set of people we are and produce. Think more about the patient and not the case. Think about trust, sympathy and tolerance and so strengthen the patient's total health care.

Herbert Rakatansky, MD

The dilemmas posed by Dr Beiser illustrate why the legal system related to malpractice requires a drastic overhaul. I agree that the family of the patient has a right to know of the mistake and to be compensated fairly for the error.

Under the present system the entire career of the physician involved with any "bad outcome" is placed in jeopardy. The existing system places the responsibility for every mistake, including the financial liability for compensating the victim, on the physician. The amount of this liability is not predictable and varies from zero (in cases where the potential dollar award is small and lawyers will not get involved) to outrageous amounts in certain cases which appeal to a jury's emotions. Is it any wonder that a physician would hesitate to report such a mistake to the family and place himself under this pall? Would any physician

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report another physician when such a report might mean financial and professional ruin?

What can be done about this? Firstly, it must be remembered that doctors are not perfect and the system of medical practice is not perfect. Mistakes will be made. It is therefore necessary to design a system in which mistakes can be reported and benefits accrued from analysis of them. Feedback to individual physicians and to the system as a whole is absolutely necessary for progress. If punishment is an automatic part of the feedback the system will not work, indeed it will not even be set in motion. In an ideal system, reporting of mistakes would be to a board responsible for evaluating the quality of medical practice. In a nonpunitive system physicians observed to be practicing in a pattern which might injure patients will indeed be reported by other doctors. This has been our experience in the Impaired Physician's Committee and the Competency Committee of the Rhode Island Medical Society. Such a board would evaluate the "mistake." Is it an isolated incident in an otherwise excellent practice pattern? Is it part of a pattern of substandard practice due to illness (eg; substance abuse, etc.) or incompetency (eg; failure to stay abreast of current knowledge)? Is it the result of inadequacies in the system itself (excessive work hours for the resident, improper labeling of the films)? Once the deficiency is identified an appropriate remedy can be applied. The doctor who has made a single mistake can be informed so that he will be more sensitive in that situation. The doctor who is sick can be treated. If treatment fails or the doctor is unwilling to be treated according to ac-

cepted standards his right to treat patients should be withdrawn. The doctor who has neglected his education should be required to remedy this deficiency to the satisfaction of appropriate authorities. If he will not or can not do this, his right to treat patients should be withdrawn.

"The doctor who has neglected his education should be required to remedy this deficiency to the satisfaction of appropriate authorities. If he will not or can not do this, his right to treat patients should be withdrawn."

The board which is doing all this work, however, should not have anything to do with the compensation of the injured patient. By separating compensation from quality control we can encourage doctors to report their own mistakes and the mistakes of others. Although only 5 reports have been received by the board many reports have been received by the Rhode Island Medical Society concerning doctors who are allegedly impaired or incompetent. Over 140 doctors have been confronted by the Impaired Physician Committee.¹ Doctors are willing to report their colleagues to the RIMS committees because they know that the feedback to the doctor will be constructive as well as protecting the public. Doctors who are unwilling or unable to recover from illness or remedy substandard practice patterns are reported to the Board of Medical Licensure and Discipline by the Rhode Island Medical Society. A system requiring mandatory re-

porting to the governmental disciplinary board by doctors of other doctors is characteristic of a police state. In those states requiring mandatory reporting of impaired physicians to the state, the committees of the medical society have been ineffectual since no one will report to anyone except under the most blatant circumstances. Most such laws have been repealed.

Patients experiencing "bad outcomes" in the medical system would be paid under a no fault system. Funding would be financed by a broad based levy. The amounts would be predetermined for a specific injury and could be related to total economic loss (not "pain and suffering"). A model system has been outlined recently by Manuel.² Patients would be assured of compensation whether their injuries were minor or major and they would be paid promptly. This is analogous to the workmen's compensation system. Fault is not required for payment for a job related injury. In return for relinquishing the right to sue, the injured party is assured of adequate and timely compensation. In countries where this type of system is in effect patients prefer it to the option of going to court. Depending partly on which "bad outcomes" are funded the cost of this system will be less than we now pay and a far greater proportion of the funds will go to the injured parties (less than 50% of malpractice premiums now reach the patient!). Only the lawyers will lose anything.

Under this proposed system the chief of medicine could have told the family of the deceased patient about the mistake with knowledge that they would receive just financial compensation. He would have

been able to preserve his intellectual integrity and to transmit it to the medical student as well. He could be certain that the circumstances of the mistake would be investigated and that constructive feedback would be provided to avoid recurrences. Treatment for medical or behavioral illnesses of the resident could be given if indicated. More intensive educational efforts could be required if indicated. If the error were in the

system itself, then action in that arena could be undertaken. Work hours could be shortened. If the error were found to be part of a pattern of occurrences with no apparent remedy, action to remove the physician from patient care responsibility could be taken.

I therefore agree with Dr Beiser's thoughts regarding mistakes in the medical profession. I would urge him to support changes in the legal system

which will make such reporting possible and bring us closer to the ideal ethical world in which truth is served, honesty is preserved and financial costs to society are reduced. Patients, physicians and society will be the beneficiaries.

¹ Rakatansky, H. Addicted Doctors: Hope and Help, RI Med Jour 72:437-40, 1989.

² Manuel, B. Professional Liability — A No-Fault Solution, N Engl J Med 322:627-31, 1990.

Frank W. Sullivan, MD

Dr Beiser asks in his provocative article, "What should a physician do when he discovers that a fellow physician is covering up a mistake which hurt a patient?"

In the example given, Dr Beiser points out that 1) a clear mistake was made and 2) delaying treatment and resulting in a contraindicated procedure which likely caused the patient's death. I agree fully that all physicians in the chain of responsibility had an obligation to uncover and report the incident to their superiors and to the patient's family. In the private setting one should approach the offending physician himself to suggest his reporting the incident and, if declined, be prepared to report the incident

to the Board of Medical Licensure. In a teaching or organized care setting one should feel obligated to report the incident up and down the supervisory network until appropriate action is taken. Perhaps most importantly, when we ourselves err, out of sight of our colleagues, we must be willing to be candid with our patient about the incident.

As exemplified, we too often participate in a protectionist network, rationalizing our poor behavior to our benefit and the patient's detriment. What has lured our priorities away? Malpractice fears, career drive, personal finances, fiscal intermediaries, practice overhead? If we are to learn anything from this case it is from the one person in the medical chain who responded appropriately, the medical student.

He did as an individual should; he discovered an error and the tragic results and appropriately reported it in the supervisory chain. It is unlikely he was taught this in any of his medical

school courses or clerkships but more likely something he and most of our students know and understand prior to their beginning their medical studies. The powerful effects of medical modeling are apparent in Dr Beiser's example wherein the student is made to doubt what he understood a physician's responsibility to be and was given by his chief a self-serving rationalization. He was fully aware that a trust had been violated; his chief had a different agenda.

"If we are to learn anything from this case it is from the one person in the medical chain who responded appropriately, the medical student."

Frank W. Sullivan, MD, is a past president of the Rhode Island Medical Society, a practicing psychiatrist in Cranston and a member of the Brown University medical faculty.

We should all be reminded to strive for that medical student's position, do what is in the patient's best interest and the rest will settle out. We are given tremendous responsibility and

trust by the public and our patients; we need to remind our students and ourselves that with that trust comes less rather than more personal choice and privilege. While the public has always been willing to grant us our scientific expertise and specialized skills it has never granted us the kind of privilege assumed by the chief of service in the presented case. When the public becomes aware of this sort of license it

correctly demands regulation of oversight.

The medical student in our case knew what he had to do and did so at some risk to his position. The physicians in this case (intern, radiology resident, senior resident, and the chief of service), all of whom presumably at some point had the same ethics as the medical student, consistently covered up or lied.

Where did they learn this? Are we in fact frequently teaching

and modeling a self-serving ethic and morality in spite of our claims of public interest and accountability?

Milton W. Hamolsky, MD

My responses to Professor Beiser's provocative and challenging essay are based on two, separate, frames of reference, (1) the limits of my 30 months' role as Chief Administrative Officer of the Rhode Island Board of Medical Licensure and Discipline (The Board) and (2) 44 years as a physician including 24 years as the Physician-in-Chief in a large, university affiliated, teaching hospital.

The current Board has functioned, since January 1, 1987 under Title 5, Chapter 37 of the General Laws of Rhode Island, promulgated by a legislature catalyzed by the media exposé of the egregious acts of one physician and-equally-the failure of

any component of the medical profession to "do anything about it." To date, the Board has not received from any source any allegation or report of unprofessional conduct by a physician based on the kind of behavior reflected in Beiser's case report. Since our "disciplinary" functions are initiated, under statute, by such a report or allegation, the Board has not, to date, conducted any detailed investigations, held any substantive deliberations, or rendered any definitive decisions relating to (1) the failure of a physician to "tell the truth": or (2) the positive act of lying by a physician to a family when his/her error has caused significant harm ("leading to premature death") to a patient. It would, therefore, be purely speculative, as implied by Beiser, to suggest what specific actions our Board might properly take in such an instance.

Our statute empowers and directs the Board "to investigate all complaints and charges of unprofessional conduct" (some

30 wide-ranging categories of which are detailed in the statute) "against any licensed physician or limited registrant and to hold hearings to determine whether those charges are substantiated or unsubstantiated." The statute further states that "any person, firm, corporation or public affair officer may submit a written complaint to the Board charging the holder of a license to practice medicine . . . with unprofessional conduct, specifying the grounds therefore" and grants immunity from "civil liability, whether direct or derivative, for providing information in good faith to the Board pursuant to this statute. . . ."

In its continuing efforts to balance (1) its primary obligation to protect the public from actions of unprofessional conduct by physicians, (2) its concerns for due process and confidentiality for the reported physician and (3) the public's "right to know," the Board has evolved the following protocols: complaints or reports of unprofes-

Milton W. Hamolsky, MD, is Chief Administrative Officer of the Rhode Island Board of Medical Licensure and Discipline, recently retiring as Physician-in-Chief of Rhode Island Hospital and Professor of Medical Science at Brown University, Providence, Rhode Island.

sional conduct, disciplinary actions, or claims filed or settled are received in writing from an individual, a hospital, another MD, medical association, health care facility, HMO, peer review board, medical service bureau, health insurance carrier, PRO, agencies of the federal, state, or local government including the courts. A hospital must report a diminution of staff privileges of any staff physician for any reason and the Board must promptly inform all health-care facilities in the state, unless decreased privileges are for purely administrative reasons.

All complaints or such reports are evaluated by the chief administrative officer and the deputy. If the complaint appears to be substantive, it is forwarded to the MD or DO involved for clarification and response in writing. The complaint and physician response are then forwarded to one of the Investigative Committees (2 physicians, 2 non-physicians) for evaluation together with any hospital record, physician's records, relevant x-ray films, EKGs, laboratory results, outside consultations. The sub-committee may request any additional data from any source, including further consultations from outside experts in the related field, and may invite the complainant, or the physician, or both, to an informal hearing. The Board is not confrontational, and we do not have the complainant and physician appear at the same time.

If the sub-committee concludes after due deliberation of all the relevant data that there is substantial cause for a recommendation of unprofessional conduct, our legal counsel is directed to prepare a consent order, detailing the findings of fact and proposed sanctions.

The consent order is provided to the physician and his/her legal counsel, only after an interview with the physician. The physician or his/her legal counsel may request alterations of the consent order. These are then considered by the investigating committee. All proceedings of the investigative committee are kept confidential.

"In my considered judgment . . . the Board is prepared and committed to discharge its mandated responsibilities to the public and to the medical profession — firmly and fairly."

If the physician accepts and signs the consent order — and only if the physician signs — the formal vote of the sub-committee is then forwarded to the full board (the remaining 8 members — 4 physicians, 4 non-physicians) with recommendations for a sanction(s). The range of sanctions is also detailed in the statute: formal reprimand; suspension, restriction, or revocation of licensure; period of probation; submission to care or counseling or treatment by a physician or program acceptable to the Board; or participation in a program of continuing medical education, practice under direct supervision, and assessment of administrative costs. The pros and cons of the case are deliberated again by the 8 members who have been purposely kept without knowledge of any prior deliberations of the investigative sub-committee. This group may accept, modify, or reject the recommendation of the sub-commit-

tee or may ask for further investigations, outside consultations, or other information. If the Board finally votes a finding of unprofessional conduct, it directs the Director of Health to sign the consent order, which at that point becomes a matter of public record.

If the recommendation of the Investigative Committee and the final vote of the full board is no unprofessional conduct, all proceedings remain strictly confidential, and the only ones informed are the complainant, the physician, and his/her legal counsel. If the final vote is unprofessional conduct and is accepted by the physician, the consent order is published in the legal proceedings of the newspaper. The decision must also be distributed to health-care facilities of the state and must be reported to the Federation of State Medical Boards, the national organization of all state medical boards located in Texas. Under new law, the decision will have to be reported to the new National Data Bank, currently under development and implementation.

If the physician or legal counsel does not, in the first instance, accept the consent order prepared upon the vote of unprofessional conduct by the sub-committee, the Board's legal counsel prepares specification of charges for a formal hearing to be conducted by 3 of the 8 untainted remaining members of the Board. The hearing committee will subpoena any witnesses, consultants, or others requested by the physician, and both sides are represented by legal counsel in the formal hearing. The investigative sub-committee and staff do not participate in the hearing or final decision of the hearing committee. The physician may then ap-

peal the final judgment of the Board, the Director, or both, by filing a notice of appeal in accordance with the rules of civil procedure in the superior court within 30 days of the decision. The Director of Health, within 20 days of the notice of appeal, must transmit to the clerk of the superior court a transcript of the record together with a certified copy of the Board's written findings. Said appeal, considered an emergency matter, shall have precedence on the calendar and shall follow the procedures set forth in the administrative procedures act, Chapter 35 of Title 42.

In my considered judgment, therefore, the Board is prepared and committed to discharge its mandated responsibilities to the public and to the medical profession — firmly and fairly.

All the legislated mandates, however, are of little value if the most knowledgeable individuals in the issues under discussion — the physicians — persist in active or passive failure to "activate the system."

The following viewpoints are my own and are not intended to represent those of the Board collectively or individually. Beiser's case is, on its face, more simple than many dealing with similar ethical issues. For, as the *a priori* bases, (1) "there is no doubt that a mistake was made," (2) "there is no doubt that the patient's death was hastened by the mistake," (3) the responsible physician actively lied to the family and (4) the student's supervisors "covered up" the mistake and the lie.

As a physician and former chief of a large medical service, I know that parallel cases do occur in Rhode Island. I have no statistical data of frequency nor do I consider it of value to play

any numbers game. I have shared in several difficult and uncomfortable discussions involving complex and imponderable variables; the "bottom line," emerging after all rationalizations and circumlocutions, remains the same — "Find some way to tell the Truth." I am aware of the claimed "mitigating circumstances," "uncertainties" of cause and effect, "gray areas" of retrospective disturbance of the family and lack of any retrospective "good," the circumlocutions of "not quite" telling the "whole truth." And I am aware of, and deeply sensitive to, the ironic and "real" fact that good physicians who reveal the truth in such instances are very likely to be — and, indeed, have been — subjected to the terrible ordeal of litigation, to further investigation by our Board with a resultant additional sanction and harmful publicity.

I am impressed by the pioneering — and sensitive — study by Novack et al. "On Physicians' Attitudes Toward Using Deception to Resolve Difficult Ethical Problems" which found that one-third of physicians responding to a questionnaire indicated they would offer incomplete or misleading information to a patient's family if a mistake led to a patient's death.¹ I recommend to the concerned reader the comprehensive and blunt summary — chiefly of legal viewpoints — of "To Tell the Truth: Physicians' Duty to Disclose Medical Mistakes" by Vogel and Delgado.² I am uncomfortably aware of the increasing criticism of medicine's "conspiracy of silence" and "cover up" and, ominously, the growing pressure for legislative action to "require" physicians (and, in Kentucky, nurses) to "report" any and all instances of

physicians' unprofessional conduct under penalty of heavy fines or "imprisonment" — or both. Beiser's pragmatic and realistic concerns, his ethically sound judgments and my interpretations of his idealistically crafted, pertinent questions of the medical profession resonate with my credo, presented 13 years ago to the Brown Program in Medicine graduation class of 1977, as follows:

"My basic thesis is that the fundamental strength of medicine has been, is now, and will always be the one-to-one highly personalized relationship of patient and his/her doctor — the individual human being in pain or anxiety or fear and the chosen physician dedicated to diagnose and cure the disease if possible, if not, to alleviate the pain or suffering or, in any event, to share and ease the discomfort of body and mind. When all the smoke of rhetoric has cleared — of politics and economics and philosophy — and when the threatening promise of the newest technology has reached its equilibrium — that interpersonal relationship, *based on trust and confidence*, will remain the final common pathway of the nobility of medicine. And I submit that it is the slippage of that noble tradition which is the root of most societal disaffection, of the malpractice crisis, of increasing interpositions of others between patient and doctor, of the growing threat of government interventions and the increasing finality of economic considerations — of the underlying unease of both the patient and the doctor in our society today."

Supreme Court Justice Harry A. Blackmun said it better — at

the February 1990 AMA National Leadership Conference; he proposed that the "first characteristic important to physicians (and lawyers) is truth, which should be at the heart of scientific investigations and medical practice."

References

- ¹ Novack, DH et al. On Physicians Attitudes Toward Using Deception to Resolve Difficult Ethical Problems. JAMA, 261, No. 20, 2980-2985, 26 May 1989.
- ² Vogel, J and Delgado, R. To Tell the Truth: Physicians' Duty to Disclose Medical Mistakes. UCLA Law Review: Vol 28:52, 53-94, 1980.

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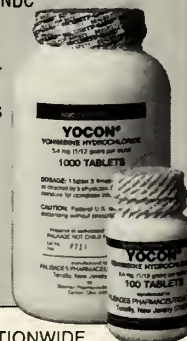
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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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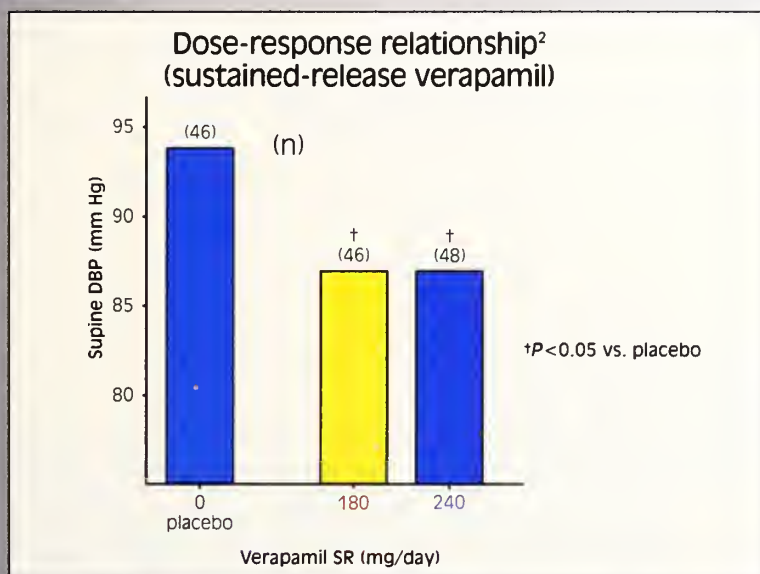


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Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration.

Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°, 2°, 3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomastia, increased urination, spotty menstruation, impotence.

References:

- 1988 Joint National Committee: The 1988 report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1988;148:1023-1038.
- Data on file, G.D. Searle & Co.

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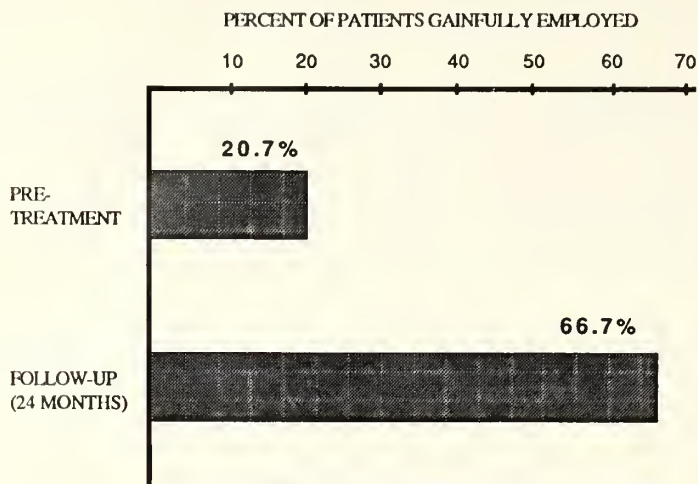
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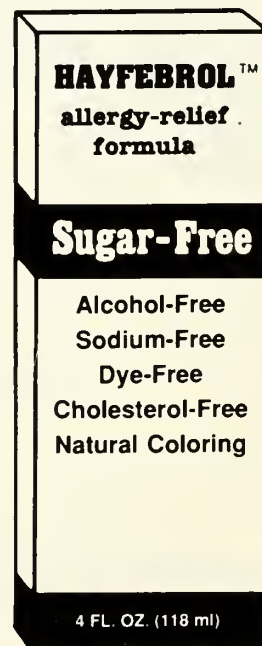
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"I Do Not Want To Be Resuscitated": A Case Report

Case Summary: Mr E.W., now 84 years old, had witnessed the terrible, slow death of his wife whose brain damage had been sustained during a resuscitation attempt following a heart attack. This experience left him convinced that it should not happen to him. He shared his resolve with his children and personal physician, telling them that if he ever had cardiac arrest, he should be allowed to die.

In May of 1988, because of chest pains, Mr E.W. was admitted to a hospital coronary care unit. He told his attending physician that should his condition deteriorate, he did not want to be resuscitated. These instructions were duly entered into the

patient's chart. Three days later, he developed ventricular fibrillations and "a nurse applied electrodes to his chest and revived him," as reported in the *New York Times* of March 18, 1990.

Mr E.W., a deeply religious man, survived the episode and now, two years later, lives in an Ohio nursing home suffering from an array of neurologic and cognitive deficits which appeared immediately after the resuscitation procedure of May, 1988. He is presently described as deteriorating, emotionally erratic, abusive and paranoid. He has recently brought suit in the County Court for "wrongful life," charging the hospital with "negligence for failing to follow

his instructions, and with battery for giving him a jolt of electricity without his authorization." Mr E.W., despite his cognitive problems, is deemed to be sufficiently competent to sue.

(Ed Note: In May of 1990 Mr E.W. died in the nursing home that had been his residence for the past two years. The status of his law suit has not been revealed in the newspapers.)

Louise S. Kiessling, MD

The case of Mr E.W. presents 2 central dilemmas. First, there is the issue of how to implement Mr E.W.'s desires. He has chosen, during a period when he is totally rational, not to experience what he has observed in his wife, namely a slow, debili-

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tated life of suffering which took its toll on her and her family. This is a choice supposedly available to most of us in hospitals which provide for Do Not Resuscitate (DNR) orders or implementation of so-called Living Wills in states which permit such choices.

Secondly, there is the issue of whether there can ever be "wrongful life." Is it possible morally or ethically ever to have "wrongful life?" Isn't all life sacred, regardless of the handicap? What of Schweitzer's Rev-

erence for Life? Aren't we as members of the helping professions bound to prolong life? Nurses, physicians, hospitals — we all see ourselves as promoters of treating, healing, curing. How can we be party to ending life by not doing all that is in our power to help our patients?

<p>ABBREVIATIONS USED: CCU: Coronary Care Unit DNR: Do Not Resuscitate ICU: Intensive Care Unit</p>

If we believe patients have the right to make such choices, then we as the medical profession must find ways to meet their needs without violating or, over time, lowering our own moral and ethical standards.

As medical personnel, we have often entered the field because of the desire to help. We are trained to respond to the earliest sign of an emergency almost by reflex.

How are we to deal with the patient's desire not to be resuscitated? We need clear guidelines developed with the patient, family and staff. The physicians and nurses need to work out with the patient and family what specifically the DNR order covers. It may seem inappropriate to a nurse in an ICU not to resuscitate a patient who is alert, rational, and fully in control of his senses as Mr E.W. apparently was at the time of the ventricular fibrillations.

The staffs of ICUs and other medical facilities need to be educated about DNR orders and the place of Living Wills in medical care. At the same time, medical personnel need to be free to remove themselves from cases where they feel their own moral and ethical beliefs may be compromised. It is vitally important that we not be forced to go against our own standards, lest we lose our sense of the value of life.

"Is it possible morally and ethically ever to have 'wrongful life?'"

I find the idea of "wrongful life" very disturbing as a concept. Who is the person who decides what is a wrongful life? What are the criteria? Will this concept, for example, expose the very elderly to non-intervention, re-

gardless of their own desires? On the other hand, resuscitation in the case of Mr E.W. resulted in his having more years of suffering than he might have had. He has seen his life become what he abhorred. It seems to me the charge of "negligence for failing to follow his instructions" may be sustainable, but I have trouble accepting the charge of "battery" when the nurse was doing what she was trained to do and believed in.

Whether my feelings as expressed here are in any way reflective of legal precedent, I don't know. There are no simple answers. We promise to "do no harm," but we cannot always prevent suffering. Is it our obligation, however, to collaborate with a patient who wishes to end his or her own suffering?

Reverend Rebecca L. Spencer

"Pastors ought . . . to present death clearly and to nurture the thought of death. They ought also to be critical of the medical-technical death-ritual. Since we live with death, we ought also to think of it while living. To settle accounts, to draw a balance, is

Reverend Rebecca L. Spencer is the Senior Minister of Central Congregational Church, Providence, Rhode Island.

important and useful. The pastors should make it clear that it can be anyone's turn next; that everyone's turn comes at some point; that to prepare oneself is good."

Peter Noll, Swiss law professor, son of a pastor, wrote those words in his journal, *In the Face of Death*. Learning he had cancer, he "decided to refuse treatment for the rapidly developing disease, feeling it would only

deprive him, by slow degrees, of his liberty and integrity, forcing upon his friends and family the burden of making choices for him."

In looking at the case of E.W., the central dilemma is how to define, sustain and protect human life in its wholeness. In analyzing such a dilemma, each participant in the event must be as clear as possible about his or her personal rules of conduct. Beyond understanding one's

accepted norms and values, I mean by this an open review of our past decisions and a determining from these actions what our rules actually are and have been. Our beliefs are revealed in what we do, and we need to be clear about what values are at stake.

Modern medicine with its new technologies has created complex medical dilemmas. The financial, societal and psychological costs of extraordinary life saving procedures, measurements of the quality of life, one's religious convictions over the control of one's life, personal autonomy and the role of hospital staff, the Great Commandment, "Thou shalt not kill" and whether it also means "Thou shalt prolong life" — these are but a few of the conflicting values and principles.

The goal here must be to analyze what has been done this time and what should be done next time. Physicians, clergy, patients, hospital staff members, families, all must recognize that they are making value judgments, and that these may collide. Honest review of the principles assumed and the actions taken will make a difference for future decisions.

Next, we need to see who else will be affected by the decision. A rigorous respect for the consequences must be nurtured by all concerned. When faced with a situation such as this where ethics and values may conflict, it also is important to be humble! Looking back at our past actions requires us to see what we have actually done rather than what we professed we would do and protects us from what has been called the "ethical superiority of the uninformed."

Whether this lawsuit wins or loses is less important than con-

sidering the question: "Can the patient's personal decision override 'normal medical procedures?' " His convictions, his desire to have control over his life and death are in some sense at odds with normal medical practices. Today's medical communities must continually assess these conflicting claims.

Measures that might be taken include an understanding by all concerned that professionals are "tools" to be used, with certain limits, by their constituents. The thorny part is defining the use of these tools and determining *who* defines these limits. To make physicians overly fearful of lawsuits hampers their professional judgment but to let patients have no say in situations where values collide is dangerous. Patients' convictions will at times conflict with physicians' personal beliefs and professional obligations. In those situations, the patient's considered conviction must be honored.

"In a perfect world, hospitals would be such model communities that each patient and each professional would be totally aware of the commitments, values and constraints of the other."

In a perfect world, hospitals would be such model communities that each patient and each professional would be totally aware of the commitments, values and constraints of the other. In such ideal circumstances, communication would have no gaps, and so this misunderstanding or non-under-

standing simply would not occur.

Rules need to be set forth and followed as clearly as possible by individuals and communities. The challenges to our assumptions occur when rules collide. This opens the door to new ways of thinking and acting. We must make decisions knowing each decision is the best we can make with information available at the present time and that others may disagree, but that such decisions and events are a part of a process of living and dying in community.

As a pastor, I feel strongly that Peter Noll's perspective must be lifted up, in the case of E.W. and in general. There is no event simultaneously so personal and yet so public as one's death. It is our task, clergy and physicians working together, to continue to delineate just how we honor the life and death of persons in our care. There can be no universally correct maxim, only individual cases, each thoughtfully and lovingly evaluated with the best professional expertise possible coupled with open communication and personal commitment.

Patients' refusal of medical or surgical treatment is an increasingly common phenomenon as patients react in fear to impersonal hospitals. The technological explosion prolongs both life and dying. At times physicians' responses to this challenge of their healing or helping role are extremely negative. The unfortunate adversarial role which then ensues is all too often antithetical to the traditional values of medicine. As in this case, legalities begin to interfere with medical judgments. Lawsuits, or threats of suit, real or imagined, begin to enter into the decision tree.

The suit occurred here because Mr E.W. had declared his opposition to cardiac resuscitation. Having gone through the experience with his wife, he saw resuscitation as cruel. At 84 he wanted to preserve some control over his destiny by expressing his wishes before the time when perhaps he could not do so. Repeatedly in geriatric psychiatry one hears patients express the fear that autonomy or control will be lost. One becomes convinced that autonomy is the irreducible core of each person's identity. The elderly feel strongly that when they lose the power to determine the course of their life, they lose that which makes life worth living. Mr E.W. acted on

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personal experience. He had not read the recent literature which makes it painfully clear that, even from a medical perspective, resuscitation is a procedure in the elderly which needs re-evaluation. In and out of nursing homes it has a yield of any quality as low as 11%.¹ Furthermore, as clarified in Murphy & Murray in 1989, tragic sequelae are all too common.² There are medical reasons for questioning the efficacy of CPR on the elderly.

"... it [is] painfully clear that, even from a medical perspective, resuscitation is a procedure in the elderly that needs reevaluation."

Beyond these medical reasons for questioning the nurse's actions in the case of Mr E.W. are the even more basic ethical considerations. E.J. Cassell³ has said that the primary role of medicine is the restoration of autonomy. Is medicine ever justified in wresting autonomy away from the patient in the interest of prolongation of life? Acting on the principle that prolongation of life is basic to medical care, the nurse in the case of Mr E.W. initiated resuscitation. She apparently forgot the instructions entered into the chart. Courts have firmly established the right by patients to establish a "code status." It does appear that many physicians and nurses still are unsure of this "right" and feel a conflict

with the value of preservation of life, at any cost, financial or personal.

In order to prevent such a tragic violation of a patient's apparent competent instruction, it is clear that conversation between patient, physician, and treatment team is necessary. Management and acceptance of treatment refusal is totally dependent on the establishment of understanding by exploring the meaning of the refusal.⁴ The central dilemma of whether treatment refusal is suicide or a competent choice can only be resolved by such exploration. This is too often avoided in our increasingly impersonal health care system.⁵ The tragedy is not just the outcome, but the fact that a patient's expressed wishes were ignored. Professional license is not license to violate choice. A better outcome would not change this essential reality.

References

- ¹ Applebaum GE, Kenz JE and Finucane TE: The outcome of CPR initiated in Nursing Homes. *J Am Geriatric Society*, 38:1992-2000, 1990.
- ² Murphy PJ, Murray AM, Robinson BE, Campion EW, Outcomes of Cardiopulmonary Resuscitation in the Elderly. *Ann Intern Med* 111: 199-205, 1989.
- ³ Cassell EJ, The functions of Medicine. *Hastings Center Report*, 7:16-19, 1977.
- ⁴ McCartney JR, Management of refusal of Medical Treatment. *Inter J of Psych in Med*. Vol 15(1). 1985-86: 31-36.
- ⁵ McCartney JR, Refusal of Treatment: Suicide or competent choice? *General Hospital Psychiatry* 1, Vol 1, (4): 338-343, 1979.

I expect that Mr E.W. is destined to endure his existence rather than anticipate release or compensation. Here is a dramatic example where a patient's desire to retain control crashes through one of the gaping holes in the technological safety net designed in good faith to preserve life. The dramatist's rhetorical cry, "Whose life is it anyway?" and the physician's lament that her range of responsible choices is limited are part of a rising Greek Chorus giving voice to the growing tragedy of lives saved that end up ruined.

There are, of course, many men and women whose sad plight resonates to the phrase "wrongful life." Any clergy person has encountered the homeless, the abandoned, those in despair, and those who have lost their way in the world. Some such souls might even say Mr E.W.'s life is a kind of metaphor of the rage they feel for the unfairness they experience. More than once have I heard: "Living hurts. Death has got to be better than this!" It is hard to counter such an argument. George Santayana was right: "That life is worth living is the most necessary of assumptions and were it not assumed, the most impossible of conclusions."

I don't know how to convince someone that their humanity is of essential worth any more than I can explain the mystery

of those whose spirits have transcended the same physical and emotional burdens that make the Mr E.W.s of the world want to end it all. In fact, caregivers have witnessed many cases of drastic illness where miraculously hope and meaning were salvaged and a sense of personal integrity maintained even in the face of impending doom.

"We are not always the best judges of the worth of life. From my faith perspective there is a special abhorrence when a society judges which impoverished lives indeed do deserve to be over."

The judgment that one's life does not have enough quality to be maintained is so subjective that often one does not take into account the desires of others. A colleague reports the following: A few years ago a woman came to my office. Her mother, a proud and vain woman in her mid-70s had taken an overdose of sleeping pills. She had feared aging — what she called the loss of the quality of life. The woman was distraught. "Mother never trusted me. I wanted so much to bring her into our home. I wanted to support her as she had supported me. She never gave me a chance. There was so much I wanted to talk about with her, so much we could have done and now all this is

denied me. She never trusted me."

We are not always the best judge of the worth of our life. From my faith perspective there is special abhorrence when a society judges which impoverished lives indeed do deserve to be over. The ashes of the Holocaust are still mixed with tears of our generation that silently witnessed a demonic Nazi bureaucracy decree who should live and who should die.

More to the point of this case summary, many of us do have opinions about *how* we want to die. Regrettably few express those feelings in the form of a Durable Power of Attorney. And, of course, a covenant of trust with a caring physician is what we expect will ultimately determine how we will be guided and guarded through our final rite of passage. What is frightening about Mr E.W.'s experience is that it is a stark reminder of the vagaries that cause the terms of that covenant to be violated. What happens if we are rushed to a strange emergency room? Who will read instructions, who will review records?

The legal system offers no answers. We depend on the medical profession to begin asking the right questions so that our legitimate rights to dignity can emerge from a calculus of competing claims.

Rabbi Leslie Y. Gutterman is Senior Rabbi of Temple Beth El, Providence, Rhode Island.

This patient's law suit is consistent with our society's penchant for seeking redress of wrongs through litigation. The competent patient has the right to refuse any therapy. The health care provider has an obligation not to impose a therapy against the patient's will. In that context and the fact that the therapy "saved his life" is irrelevant. Or is it?

If the "life-saving" therapy was administered inadvertently, the suit heads in one direction; if administered knowingly against his will but out of an employee's conscience, the suit leads in a slightly different direction. These facts could be important but are not the central issue for discussion.

The problems in this case open many confusing doors for the courts and the health care providers.

Since a hospital staff has been trained to save lives whenever possible, directions to the contrary run against the grain. "Do not resuscitate" orders are not uncommon and are respected. The patient's medical condition is usually well recognized as the justification for the DNR order. Where the wish to not be resuscitated is based less on the patient's current condition and more on fear of a future outcome, the staff is less likely to be "tuned in." In the current case, did "ventricular fibrillations" constitute a deterio-

rated condition or merely a readily reversible arrhythmia? An otherwise stable patient developing "ventricular fibrillations" is a prime candidate for salvage and, if residing in a CCU, is especially prime. Failure of CCU staff to let a patient die, with interventional equipment immediately available, is understandable. The patient's unsatisfactory outcome was difficult to predict.

The patient's (claimant's) *life* is now a potential source of damages (not his death). Since the life can be modified or ended (unlike a "wrongful death"), the claimants future health and related health issues take on complex significance.

"Is a person leading a 'wrongful life' any different from a person leading any other life? Are those subsequently providing care extending a 'wrongful life'? Are those denying care assisting the patient in achieving his initial desire?"

On the surface, there is a simple issue of failure to carry out legally-binding instructions. Under the surface are many issues regarding life, health care delivery and litigation which are tortured and complex. Is a person leading a "wrongful life" any different from a person leading any other life? Are those subsequently providing care extending a "wrongful life?" Are those denying care assisting

the patient in achieving his initial desire?

Who is legally and financially responsible for this patient's future care? Is the life-saver (hospital, nurse, etc) now liable for costs (and complications) attendant to any *future* treatment aimed at *improving* his condition? Has the patient become their dependent since his "life" is now on their economic conscience?

There is little question that an individual's explicit wishes were circumvented and that he has suffered. The question at issue is whether the act of "saving his life" is any different than the violation of any other agreement.

If his physician appeared on the scene shortly after defibrillation, would he/she have been obligated to turn off assist devices in order to bring the situation into closer compliance with the patient's wishes?

When one enters the health care system, it should be recognized that it is a system heavily weighted toward saving lives and treating illness. To expect such a system to function as well in reverse is an unrealistic expectation. The patient's rights should not be reduced in this setting. Legal remedy is still his right. The court, however, should recognize the nature of the health care system and modify the expectation that all patient wishes can be complied with to their satisfaction in such a system.

Similarly, patients must be made to understand the limitation inherent in such requests. The physician must assume this educational role when caring for such a patient.

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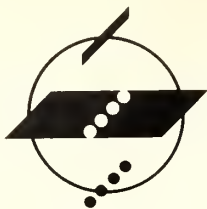
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"Am I My Brother's Keeper?": A Case Study

Case Report: A young woman physician works in a large and busy municipal hospital, employed as a resident physician in internal medicine. In the course of her work she inadvertently punctures her skin with an intravenous needle contaminated with the HIV virus, the causative agent of AIDS. She immediately notifies the hospital administration and she is periodically tested for serologic conversion. Within a short time she is sero-positive for HIV infection and later develops the signs and symptoms of active AIDS. She now sues the city, the municipal hospital and some of its physicians for large sums of money.

* * *

This case and its moral ramifications formed the basis for an evening discussion before the combined congregations of St

Martin's Episcopal Church (Rev D. Burke), Central Congregational Church (Rev R. Spencer) and Temple Beth El (Rabbi L. Gutterman). The discussions were conducted by Professor Gewirtz and Drs Fretwell and Scott. Their commentaries follow.

The case was placed within the framework of the first book of Moses, called Genesis, which tells of the birth of Cain, a tiller of the ground, and later his brother Abel, a keeper of sheep. And when the Lord regarded Abel's offerings more favorably than his, Cain became angry. Cain said to his brother: "Let us go out into the field," and there he slew Abel. Then the Lord said to Cain: "Where is Abel, your brother?" Cain replied, "I do not know. Am I my brother's keeper?"

The discussants were asked to consider the current case as

an extension of the question, "Am I my brother's keeper?" Furthermore, they were asked to consider some corollary questions: "Am I my brother's *only* keeper?" And how do I reckon my share of this responsibility? "Am I my neighbor's keeper?" But what if my neighbor wants no keeper? Are there rules to tell me when to be committed and when to be indifferent to another's plight? "Am I the stranger's keeper?" "Am I my own keeper?" And ultimately, who is the keeper, who is responsible for this physician now infected with the virus of AIDS?

Nancy H. Gewirtz, PhD

An equally compelling question is, "Why are we having this discussion?" Surely, as an enlightened society we have come to some consensus about this issue. Yet, one only needs to take a look at US social policy to recognize that conflict over this question has simply never been resolved. While, we as a nation,

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take our Judeo-Christian heritage to heart; that is, we do believe we have some moral responsibility to care for each other, we also are equally committed to the value that, "God helps those that help themselves." The notion of individual responsibility for success or failure is firmly entrenched in the Protestant work ethic and our culture. As such, historically, most of our societal attempts to deal with health and welfare problems have been compromises that attempt to

address both of these conflicting value positions, resulting in a halting, fragmented and largely ineffective response. Unlike our neighbor to the north, and most other industrialized nations, we do not have a comprehensive health care system that provides access to all. We know, for example, that 37 million Americans have no form of

ABBREVIATIONS USED:
AIDS: Acquired Immune Deficiency Disease

health insurance. Unlike, Canada, Sweden, and France, we also do not have a comprehensive family policy that provides on-going supports such as day care, family allowances, parental leave and on and on. The question of societal vs. individual responsibility remains controversial and a deterrent to effective policy.

Where does this ambivalence leave us when we are confronted with AIDS, an epidemic with political, social and cultural meanings that go way beyond the disease itself? It leaves us on a battleground of high-pitched moral debate over whether we as a society are "our brother's keeper," instead of addressing the dire public health consequences of this disease for us *all*. No matter how much we attempt to respond to this epidemic by making moralistic judgements about people's behavior, the reality is we cannot be separated from each other. Society is a series of relationships that make up the fabric of our existence. Never has this been clearer than it is with AIDS.

A brief look at some examples of these inter-relationships will help us understand why we will fare far worse than necessary with this disease if we continue to attempt to polarize the issue into a moralistic "we-they" scenario. First of all, the Dr Prego case can be viewed not just as one individual's tragedy. This situation has been viewed by some as a labor-management issue. If, as the recent settlement suggests, the hospital has been negligent in providing appropriate education, procedures and equipment to protect its workers, what can be concluded? Was it the individual worker's fault? Clearly, not entirely. Why then has the hospi-

tal not done a better job? Many have argued that the health care system has been very slow to react to this epidemic primarily because of a disdain and fear of those who have initially suffered the most. Clearly, gay men, drug users and blacks are not this nation's favorite citizens. But then an "innocent" victim, a Dr Prego or a hemophiliac child, who receives an AIDS-infected injection, contracts AIDS and now we wonder why the health care system did not take better care of these worthy workers and patients. If we continue to conceptualize AIDS as caused by individual immoral behavior, rather than as a communicable disease, attempts to protect health care workers as well as all Americans will be hampered by a lack of funds and commitment.

"Who then is to decide addiction to illegal drugs is a moral issue and not a disease beyond the control of the individual?"

And what of the legal relationships and responsibilities in this case? Dr Prego and her lawyers appear to have won. New York City must now pay them over a million dollars. Clearly, the individual interests of the client and lawyers have been served, but what of the public good? Clearly, Dr Prego and her family should be compensated for a life tragically cut short since culpability appears to have been determined. But are these million dollar individual awards actually contributing to the problem? If society does not like spending money for AIDS treatment of gay men and drug

addicts, what about the growing number of children with AIDS, or unsuspecting sexual partners who get AIDS? How many of these people could New York City help with a million dollars? How much prevention could be provided with that kind of money? The lawyers, plaintiffs and defendants in the Dr Prego case were not engaging in the resolution of a private, individual trouble, for the outcome has a significant impact on the prevention and treatment services that may be available for all New Yorkers.

And what about the economic relationships which contribute to the spread of AIDS? Is the use of intravenous drugs, and the subsequent sharing of needles which transport the disease, totally the responsibility of the individual? Our national leaders in politics and business want us to view drug use as a morally reprehensible individual act. But where do the drugs come from? Illegal drugs are a big business and we do not have to look further than Noriega to find that when it has been useful for the United States, these same politicians and financial entrepreneurs find themselves in "the" business. And while AIDS appears to be stabilizing itself in the gay community, it is running rampant in the inner city minority communities, where poverty, discrimination and despair make the residents easy prey for the drug business. The Secretary of the Department of Health and Human Services thought R.J. Reynold's marketing of "Uptown" cigarettes to blacks was simply immoral. How different is that than the marketing of illicit drugs in the very same neighborhoods? The economic benefits reaped from drugs are not realized by the average intrave-

nous drug user but rather, as we have learned through many recent exposés, by powerful political and business interests. Perhaps public policy should dictate that all those people who directly or indirectly benefit from the drug business should not be provided treatment if they become ill, because of their immoral behavior.

Finally, what about the relationships between people in a pluralistic society such as ours? Who is to determine which individual behaviors are morally acceptable? Who, for example, is to decide that homosexuality is immoral? The American Psychological Society used to view homosexuality as deviant, not any longer. It used to be that some thought it was immoral for women to work outside of the home. Now, we've changed our minds. Similarly, alcoholism used to be viewed as immoral behavior. Now it is viewed as a disease. Who then is to decide addiction to illegal drugs is a moral issue and not a disease beyond the control of the individual? Some of these

changes in attitudes have come about because we have learned that these moralistic approaches are not helpful to the individuals involved nor to the society as a whole. Tragically, these same kinds of moral judgments about sexuality and drug use have curtailed the implementation of the two most effective and efficient approaches to slowing the spread of AIDS that are presently available to us. Explicit sex education, has been rejected by many because it is viewed as encouraging sexuality in general and homosexuality, specifically. According to the US Office of Technology Assessment, in 1986 the Communicable Disease Center had only \$25 million available for education but 3 times that amount was needed for the program to be effective. Free needle exchange programs, to curb the spread of the disease have similarly been dismissed as condoning drug use. Clearly, trying to curb the spread of AIDS by stressing the need to control individual morality has failed as a public health measure. The sad reality is

that probably everyone of us knows somebody with AIDS. We cannot control the spread of this disease by trying to convince ourselves that it is not our problem. For no matter how hard we want to cry out, "They," "them," "those people have a self-inflicted disease and are getting what they deserve," this is an epidemic that can kill anyone and if we continue to approach it as an individual failing of those people and not a societal responsibility, we will continue inadvertently to contribute to the spread of that which we are trying to avoid. It is not just bad grammar in a democratic society, but a prescription for disaster, to think we can survive without a commitment to "we." We can try and point our fingers and declare this is their fault because of their immoral lifestyle, but like it or not we are all connected in a fundamental series of relationships. If we are to survive this epidemic, we must all be each others' keeper.

Marsha D. Fretwell, MD

This essay is written in response to a recent event in the history of the profession of medicine: a staff physician has

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brought a lawsuit for a very large amount of money against the hospital where she, in the process of delivering direct care to a patient, contracted the AIDS virus. The focus has been shaped by the question, "Am I my brother's keeper?", the title of the meeting in which I first addressed this topic. I respond to this question and the recent event from my viewpoint as a

physician who cares primarily for older patients in the American health care system of the 1990s. I am specific about this viewpoint because, as a physician who speaks prospectively with her patients about their desires about managing their death, I practice a style of medicine that is mainly nontechnological and perhaps resembles the practice of physicians of the

1950s or 1960s more closely than the highly specialized and technologically oriented practice of physicians today. My focus on frail older patients has "protected" me then, not only from an excessive involvement in technology, but also from the situation of caring for individuals whose diseases are contagious as well as life-threatening.

Although disseminated tuberculosis was still a frightening reality in my residency, personal safety in my practice today prevents me from being able to truly share the experience of the staff physician described in the opening sentence. Additionally, my research investigations suggest that the process of treating acute illnesses of frail, older patients in the hospital may actually cause a decline in their physical, emotional, and cognitive function; a finding that has cooled my enthusiasm about the medical applications of technology and has distanced me somewhat from the high costs and financially driven structure of our health care system. As I have sought other solutions to improve health outcomes for older patients and to prevent the harm of our current system of care, I find myself rediscovering approaches to patient assessment and care that I would now describe as the art of medicine. These include: the essential role of the healing relationship, the power of the physician's intuitive cognition, the importance of the family as a model for caregiving and nurturing the vulnerable in our society and finally, an understanding of the frailty of human nature in the face of perverse incentives.

Am I my brother's keeper? Certainly, within the traditional values of the profession of medicine there is a place for caring

for one's brother, regardless of one's perception of his value. Cain asked this question of Yahwah, after he had slain his brother out of resentment, jealousy and anger. Abel was the light of life for his parents and apparently, also for Yahwah. The story of Cain and Abel is the story of human nature with its potential for hate and love, death and life or evil and good to exist within the same human being. Likewise, within the profession of medicine, there exists the potential for using our increasing knowledge for both good and evil. Technology is merely a concrete or material extension of our knowledge and as such may be used in good and useful ways or in painful, degrading ways. Because technology appears to always represent progress or hope and its application is more easily quantified than applications of the art of medicine, our focus on the specialized and technical aspects of medical research and care have overwhelmed and almost obscured the interpersonal and healing nature of the profession.

The most insidious effect, I think, of the current trends in the structure and practice of the medical profession is the separateness and lack of genuine interpersonal involvement or connectedness that pervades the day-to-day activities of the profession. Not only does this separateness undermine the patient-doctor relationship, but it also stresses the doctor-hospital relationship, perhaps leading to communication barriers and lawsuits. Is there and should there be a difference between the environments of patient care and industry? Is the stick of a needle from an ill patient similar to a low-back injury or being struck by a piece of

poorly maintained machinery? These are important but secondary questions that arise as we pursue the fiscal or free market approach to containing health care costs further and further without ever discussing, as a society, the basic question: Who do we want physicians to be? Should they be caretakers or technicians?

"That (Hippocratic) oath marks the original commitment of the medical profession to use its healing powers only for the good of the patient and explicitly acknowledges that these powers could be used for harm."

To me, it is the healing relationship formed by two individuals, one with a problem or a pain and the other with a capacity for empathy and the courage to apply it, that defines the original core out of which our current medical profession has evolved. Healers are and have been present in all cultures throughout history. The Hippocratic oath represented one important transition as the profession of medicine has differentiated and has evolved away from other types of healers. That oath marks the original commitment of the medical profession to use its healing powers only for the good of the patient and explicitly acknowledges that these powers could be used for harm. Here we may view the situation of Abel and Cain as a representation of the potential in the profession to bring both good and harm to patients. From this point of view, however, the behavior is

channelled exclusively toward good by clearly stated professional values. What are the values of our profession today? How strong are the professional ties and collegial relationships? How far off center can the caring or healing relationship be moved by financial concerns

without destroying the profession? The patient and the biology of human health and disease is the centering force for medicine. It is through responsible, yet caring relationships with ordinary, frail, vulnerable and perhaps personally threatening patients that the art and

science of medicine are best brought into balance. We must be our brother's keepers, for it is through this mutual relationship that we confront and accept our own frailty and thereby remain in connection with the universe of all human beings.

H. Denman Scott, MD

Am I my brother's keeper? We are asked to take this ancient and haunting biblical question and apply it to our modern context. We are asked to consider what is society's responsibility to persons whose risky behavior invites, but does not guarantee, premature illness and death. Framed another way, should people who smoke, engage in dangerous sex, indulge in a fatty diet, and fail to exercise regularly pay a financial surcharge for their bad habits? Should they be subject to social sanctions? We hear an increasing number of calls for such action. I find myself troubled by such proposals. Several perplexing questions come to mind:

1. By imposing charges and sanctions, are we inappropriately blaming the victims of terrible suffering and disease? Is it bad to do so?

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2. What do we do about persons who die suddenly, perhaps prematurely, but who impose no cost to society by way of medical and rehabilitative care? Should their estate get a rebate on the individual's "bad habit" fees?
3. What do we do about people who escape the consequences of bad habits? At a recent state house reception for centenarians I met a lady of 107, who upon lighting up a cigarette, asked if I would advise her to quit smoking, a habit she had pursued for no less than 75 years!
4. What do we say to people who live an impeccably healthy life, but develop cancer or some other disease prematurely? Should they get a special bonus for bad luck?

To extend our thinking on these questions it is instructive to consider the risks of dying that occur among smoking and non-smoking men. Table 1 outlines what will happen to 2 cohorts of 35 year old men.¹ In

each age interval (young middle age, middle age, and elderly) the smokers suffer considerable excess mortality. The absolute risk of dying is much less among the young than the old. However, the relative risk of dying is greatest among the young, 3.1, compared to the old, 1.3. Overall, many more non-smokers, 563, survive to the ninth decade than smokers, 301. Not to be overlooked in this good news for non-smokers, is the bad news that non-smokers still die in fairly large numbers prior to the age of 80.

Woody Allen has noted that dying is a good way to save money. In this vein should we, rather than penalizing the smokers, consider instead rewarding smokers who "check out" before age 80? By dying earlier than they otherwise might, these people reduce the call on Social Security trust funds and reduce the numbers of persons who develop the serious disabilities of great age such as Alzheimer's disease.

Another aspect of the question needs discussion. Are some people more likely to pur-

sue a healthy lifestyle than others, and if so, what are some of the reasons for these differences? Three come to mind:

1. Education and economic well-being provide the basis for a comfortable and interesting life, one which is worth living. Persons in such circumstances usually look forward to long life and are willing to abstain from smoking, to follow a proper diet, pursue regular exercise, etc in order to reduce their risks of premature illness and death.
2. Genetic predisposition to addiction makes some people more vulnerable than others to becoming habitual users of a variety of addictive substances from tobacco to cocaine. Most of us have observed individuals who could smoke one cigarette a day and never feel the need for any more. We have also seen many others who rapidly assume a pack per day habit. Concerning alcohol, there are many family studies which show that various members from one generation to another fall victim to obsessive alcohol use. Many scientific questions in this area are currently being pursued and have promise for elucidating the physiologic basis for addiction and for developing treatments. We must not lose sight of the point that a person's genes probably play an important role in whether he/she goes from rare experimentation to compulsive use.
3. The cultural and religious environment into which one is born also has a powerful influence on a person's future lifestyle. In many traditions, it is wrong to smoke, to

Table 1

Deaths Between	1000 Smokers Age 35	1000 Non-Smokers Age 35	Excess Deaths	Relative Risk
35-50	55	18	37	3.1
50-65	223	94	129	2.4
65-80	421	315	106	1.3
Total	699	427	272	1.6

Source: VR Fuchs: HEALTH AFFAIRS, Winter 1983, 2(4). p. 56-69.

drink alcohol, to be sexually permissive. For young people who embrace the tradition and follow its dictates, we have powerful evidence that they will experience less illness and premature death. With its high proportion of Mormons, we have recently learned that Utah has smoking related health costs of \$45 per capita which are almost 5 times lower than the \$240 per capita which we pay in Rhode Island.²

In my judgment it is hard to hold persons responsible for the genes they are born with, or the tradition (or lack of tradition) they are born into. We also have no choice in whether we are born to well-to-do or poor parents. As we grow and mature, more responsibility properly devolves to the individual. However, there is a fair amount of luck at play in the beginning of our lives which can determine whether we will pursue, or will not pursue, the healthy life.

What policies should we pursue to promote a healthy life? Of first importance is a sustained commitment to combat ignorance and poverty. These two forces blot out a vision of a promising future and invite people to live for the momentary pleasure of the here and now. As part of our educational efforts, we need to augment our health education in our schools

and work to create a social climate which discourages smoking, alcohol, drugs and indiscriminant sex, and encourages respect for others, proper diet, and vigorous exercise.

"These two forces (of ignorance and poverty) blot out a vision of a promising future and invite people to live for the momentary pleasure of the here and now."

We should encourage and support the basic research which will unravel the physiologic basis of addictive disorders and lead to innovative therapies.

We must be very mindful of the many cultural and religious traditions present in America. Some will have very strict codes of conduct which will promote health; others will be a good deal more permissive in how legal substances such as tobacco and alcohol are used. Some tolerance of unhealthy habits is essential if we are to help people cope with them and overcome them. Returning to an era of prohibition is not going to be any more successful now than it was in the past.

As a society I believe we have a fundamental obligation to care for sick people with sensitivity and without judgment. In

short, I believe we are our brother's and sister's keepers, especially those who, for whatever reasons, indulge in dangerous habits.

References

- 1 Fuchs VR: "Setting Priorities in Health Education and Promotion," HEALTH AFFAIRS, Winter 1983, 2(4). p. 56-69.
- 2 "Smoking and Health: A National Status Report." Report to the Congress, 2nd ed. US Department of Health and Human Services, Office on Smoking and Health, DHHS Publication # (CDC 87-8396) February, 1990.

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45	\$15.68	\$23.58	\$ 42.43
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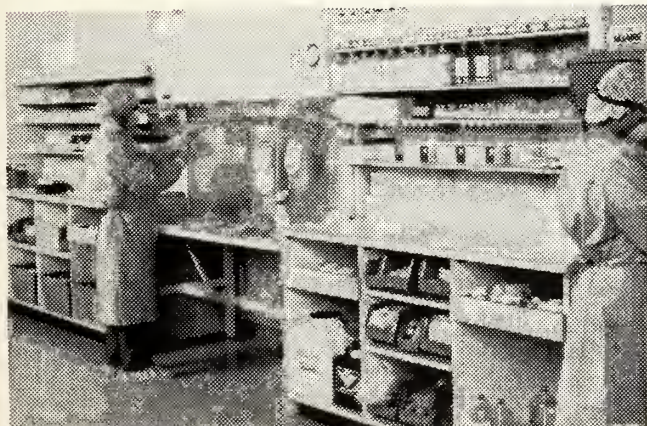
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Ethical Issues at the End of Life

David A. Ames, DMin

The pillars of our western society (erected during the Enlightenment) are crumbling.

CASE A:

Janet Adkins, age 54, a resident of Portland, Oregon, wife and mother of 3 sons, had Alzheimer's disease, which had progressed to a point where she could no longer enjoy "reading, literature and music — the things she loved most." She traveled to Oakland County, Michigan to commit suicide with a device built by Dr Jack Kevorkian. In his 1968 VW van, Janet Adkins was attached to a heart monitor and then an intravenous tube was put into her arm.

The tube first delivered a saline solution. Mrs Adkins then pressed a button that injected thiopental, a coma-inducing drug, followed moments later by potassium chloride, which stops the heart within minutes. She was unconscious in 25 seconds, and died in 5 or 6 minutes.

This story raises several questions. I will ask only two of them: Is it ethically defensible for a person to end his or her life by suicide when confronted with

an incurable degenerative disease? Should death be aided or assisted in an active manner by physicians?

CASE B:

Three months ago, on March 18th, the *New York Times* carried a story about Edward Winter, an 84-year-old man from Cincinnati, Ohio, who 2 years ago witnessed the slow, agonizing death of his wife of 55 years, who had suffered brain damage after shock resuscitation from a heart attack. This experience left him convinced that nothing like this would happen to him. He shared his resolve with his children and personal physician, telling them that if he ever had cardiac arrest, he should be allowed to die. One of his daughters describes her father as a "pretty staunch Catholic."

A few months later, in May, 1988, Mr Winter, because of chest pains, was admitted to a hospital coronary care unit. He told his attending physician that should his condition deteriorate, he did not want to be resuscitated. A "Do Not Resuscitate" order was entered into the patient's chart. Three days later, he developed ventricular fibrillations that signal sudden death, and a nurse applied electrodes to his chest and revived him.

Two days after he was revived, Mr Winter suffered a debilitating

stroke. He is now, two years later, partly paralyzed, suffering from an array of neurologic and cognitive deficits, and largely confined to his bed in a nursing home. He is described as deteriorating, emotionally erratic, abusive and paranoid. A few months ago he filed suit in the Hamilton County Court of Common Pleas for "wrongful life," charging the hospital with "negligence for failing to follow his instructions, and with battery for giving him a jolt of electricity without his authorization."

In some ways Edward Winter's situation is the opposite of Janet Adkins'. How is "wrongful life," as a result of the use of medical technology against patients' wishes, an issue for ethics? What about the cost? Not only in terms of Mr Winter's deteriorating condition, but in terms of dollars and economics? His medical bills now total about \$100,000 and are still rising, and his life savings are just about depleted. How is justice served in a situation of this kind?

In order to address the issues raised by these 2 cases, I wish first to say something about the context in which we are living today. I will then venture some remarks about 3 areas of concern: economics as an ethical issue; the ethics of death; and

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justice as an ethical principle.

The Postmodern Context

We are living today in the early stages of an era which philosophers refer to as postmodern. In this early stage, the pillars of our western society are crumbling. These were erected during the Enlightenment, and, as Diogenes Allen, professor of Philosophy at Princeton, points out, their breakdown is evident in a number of areas. Allen cites 4 areas¹:

First, "it can no longer be claimed that we live in a self contained universe." The status of the universe and our place in it have not been settled by science and philosophy. It is again meaningful to ask, "why does the universe, this one or any universe at all, exist?" What is the meaning and purpose of human life? "We have the opportunity and the task of turning people into seekers, . . . with the confidence that if one seeks one is likely to find."

A second breakdown is the "failure to find a basis for morality and society." The Enlightenment tried "to base morality and society on reason" alone, "rather than on religion." It tried to show that "moral behavior is objective and not a matter of individual choice, nor relative to a society." Today, traditional morality is bankrupt, and "we find ourselves in the time of the Judges, in which each person does what is right in his or her own sight." Perhaps this explains why a Janet Adkins and a Dr Kevorkian did as they did last week, or why a nurse resuscitates a patient against his wishes, or why questions about abortion, euthana-

sia, capital punishment, religion and school prayer are politically and socially so divisive.

"The third pillar of the Enlightenment is belief in inevitable progress." You might recall the advertising motto of General Electric: "Progress is our most important product." Well, GE doesn't use that any longer. Part of the optimism of this belief was founded on the conviction that education and science would "free us from social bondage and from nature's bondage. But there is now increasing concern that education and social reform may not be enough," and many are puzzled about what else is needed. When we look around us at the way we as a society tolerate poverty and spend our energy instead on band-aid approaches to drug control, crime control, gun control and scapegoat those things which make a difference for the good of the common-weal — for example, equal opportunity and adequate health care for everyone — we can see where the pieces of our puzzlement are scattered.

A fourth breaking pillar is the "assumption that knowledge" (which today gets confused with information) "is inherently good." We are "increasingly aware that there is no inherent connection between knowledge and its beneficial use." Note the destructive power of nuclear weapons and the abuses of genetic engineering. Knowledge carries with it power both for good and ill.

On the positive side, much of what we have learned because of the Enlightenment is beneficial. I am convinced we are better off because science and philosophy have not answered all the questions about life. If we knew the answers, life could be-

come rather monotonous or boring. And, although traditional morality is bankrupt, we are in the midst of an opportunity to fashion new moral and ethical foundations which can support a more diverse and pluralistic society and respond to the growing interdependence of our global village. Inevitable progress brought us to the brink of environmental disaster. It remains to be seen whether we have gone too far or whether we can reverse the processes of planetary destruction so directly linked to the name of progress.

. . . we are in the midst of an opportunity to fashion new moral and ethical foundations which can support a more diverse and pluralistic society and respond to the growing interdependence of our global village.

Economics as an Ethical Issue:

The issue of economics must be addressed at two levels: the micro level and the macro level. Janet Adkins and Edward Winter represent the micro level of economics. Janet Adkins, we are told, was concerned about the quality of her life more than the matter of how long she lived. I have not seen a discussion of her concern for paying for treatment and care during the course of a debilitating disease, which could last for 10 years, but one might question whether it played a role in her decision. It is clearly a factor in Edward Winter's case; his life's savings are nearly depleted.

At the macro level, our society

is questioning whether health care can or should be limited on the basis of economic considerations. A group called Families United for Senior Action is seeking national legislation to establish a system of social security for long term care. They point out that 50% of persons 65 and older will spend some time in a nursing home, that the average cost of a nursing home is now about \$30,000 a year, and that almost half of all senior citizens living alone will spend down their income and assets to the poverty level after only 13 weeks in a nursing home. Edward Winter's situation is a case in point.

Part of the reason for the burgeoning numbers of people needing long term care due to chronic conditions is that medical progress has given us a life-saving technology that often leaves people chronically ill or with a poor quality of life. Daniel Callahan, director of the Hastings Center, has argued for a principle of symmetry: "A technology should be judged by its likelihood of enhancing a good balance between the extension and saving of life and the quality of life."² The uses of technology, like CPR in hospitals, for example, should be balanced by weighing the promise of a good, long-term outcome with the lowest general cost, including personal cost to the patient and family as well as economic and social cost.

It is interesting to note that the state of Oregon, Janet Adkins' home state, passed legislation this year to address this very problem. The Oregon model is based upon several principles:

- (1) There must be universal access for the state's citizens to a basic level of health

care.

- (2) There must be a process to determine what constitutes a "basic" level of care.
- (3) The criteria used in this process must be publicly debated, must reflect social values, and must consider the common good of society.
- (4) It is the obligation of society to provide sufficient resources to finance a basic level of care for those who cannot pay for it themselves.
- (5) The health care distribution system must offer incentives to use those services and procedures which are effective and appropriate rather than those which are of marginal or unproven benefit.
- (6) The distribution system must avoid creating incentives for overtreatment.
- (7) Funding must be explicit and the system must be economically sustainable.
- (8) Allocations for health care must be part of a broader allocation policy which recognizes that health can only be maintained if investments in a number of related areas are balanced.³

I think that these principles are laudable and are worthy of national debate. One of the major problems is that we do not have a comprehensive national plan for addressing the social, educational, nutritional and health needs of our citizens. It is a clear sign of moral bankruptcy that we do not use our tremendous wealth to feed the hungry or to provide adequate housing for the poor. With the ending of the Cold War and with greater international cooperation, we in this country

now have an opportunity to build a comprehensive program that will rebuild our infrastructure and respond to the social and health care needs of all our people. We must recognize that we cannot do everything; there are limits. But we can do much better for more people if we establish an agenda of national priority and develop a comprehensive plan similar to that of the Oregon model.

One of the major problems is that we do not have a comprehensive national plan for addressing the social, educational, nutritional and health needs of our citizens.

The Ethics of Death

One of the reasons for the need for hospice care in this country is that ours is a death-denying culture. Although I assume that most schools of nursing include courses about managing and caring for dying patients, I am confident that the majority of medical schools do not include courses on death and dying in the curricula, and if they do, they are most likely elective courses and are not required. We do everything possible to prolong life, and we often do not provide adequate pain medication in fear that the overuse of narcotics would kill a patient before his or her terminal disease would. Charles Meyer, the Assistant Vice President for Patient Services at St David's Community Hospital in Austin, Texas, suggests a number of cultural myths about death which are frequently impediments to good decision making at the end of life. Here are some excerpts from them:

1. *Only old people die.* "This myth can result in young people being subjected to extraordinary efforts from intubation to chemotherapy just because they are young, or old persons prematurely being denied further treatment because they are old." The fact is that "people of all ages die."

2. *Medicine can cure everything.* "The myth persists . . . that drugs, medical technology, and their physician purveyors can prevent or cure" just about everything.

3. *Life is always the highest value.* We have often heard that what is at issue is the fact of life itself, and we seem to forget that in almost every religious system longevity of life is not nearly as important as "the virtues of love, faithfulness, forgiveness and compassion." It is here that Janet Adkins may have something to teach us just as Edward Winter does.

4. *Money should not be a consideration.* We have already discussed this in our consideration of economics as an ethical issue.

5. *Death is evil. Death means failure.* Many people continue to see illness as "punishment from a wrathful God." The point is that "sickness and death have no moral value, they are amoral occurrences." AIDS, cancer, heart disease, Alzheimer's, and all the others, have nothing to do with good or evil, right or wrong, reward or punishment. The death rate has always been and remains 100%. What is good or bad about death is the manner in which we respond to it.

6. *Where there's life there's hope.* This myth is simply untrue. Often, "where there is life there is the opposite of hope — agony, fear, excruciating pain, anger, frustration, loneliness, despair. . . . Hope embraces

and affirms both life and death as parts of a greater whole of existence. Hope sees life as a mystery to be lived, and death as part of that mystery."

What is good or bad about death is the manner in which we respond to it.

7. *Suffering is redemptive.* While it is sometimes an "occasion for the healing of memories, relationships, hurts, fears or guilt, . . . suffering is also often the occasion for unquenchable bitterness, debilitating despair, collapse of faith, and disintegration of personhood. . . . Related to illness, suffering is as amoral as the virus, bacteria or bodily condition that is its cause."

8. *You don't die until your number comes up.* "This myth reduces God to the clerk in the deli section of the local supermarket." It says that we should not "make life support decisions because the patient will die when God is ready. . . . People generally choose the time of their deaths. They die around anniversaries, birthdays, holidays; and they often wait to die until their loved ones leave the room."

9. *Pulling the plug is suicide/murder.* Withdrawing hydration, nutrition or respiratory maintenance is suicide, or murder, and is therefore inhumane, cruel and immoral. The underlying assumption here is that "to take control over one's death" or to administer palliative drugs only "is to usurp the power and prerogative of a higher authority, an all-controlling God." However, "not to decide is to de-

cide." We need to learn more about how we should be responsible for others as we would have them be responsible and caring for ourselves.⁴

Kenneth Vaux, professor of ethics in medicine at the University of Illinois, reminds us that "our moral heritage condones mercy in the face of suffering, courage in the face of uncertainty, and forgiveness in the face of tragic extremes."⁵ Vaux quotes Pierre Teilhard de Chardin: "We must struggle against death with all our force, for it is our fundamental duty as living creatures. But when by virtue of a state of things, death takes us, we must experience that paroxysm of faith in life that causes us to abandon ourselves to death as to a falling into a greater life."⁶

The reason that Janet Adkin's death received such prominent attention is that many remain unpersuaded that her struggle against death was completed, except on her own terms. She was still functioning rather well, and might well have exercised the option of a durable power of attorney or a living will so that medical and life supporting treatment could be withheld when she became incompetent to make decisions for herself. Furthermore, Dr. Kevorkian, in assisting her suicide so readily, was in violation of a basic tenet of his profession. As a physician, at least in this particular relationship with a patient, he is perched on the slide of life's slipperiest slope.

Edward Winter's case is much clearer. His suit charges the hospital with negligence and battery for giving him treatment without his authorization. The hospital, in its defense, claims that saving a life can never be considered an injury subject to compensation. It seems appar-

ent that the hospital, for whatever reason, failed to honor the DNR order agreed to by the patient and his attending physician.

Justice as an Ethical Principle

Finally, what does justice require? One of the problems of our postmodern culture is that we, for lack of moral imagination, have come to rely on that which is legal as the basis for what is right. If the law permits something, it is ok. And, if there is no law to take care of a social or even a personal situation, let's make one. Our society is more litigious than ever, and as a consequence we are less trusting of one another and also of life.

One of the problems of our postmodern culture is that we, for lack of moral imagination, have come to rely on that which is legal as the basis for what is right.

Most of the recent discussions about justice have focused on what I would call Enlightenment justice. Justice is referred to as "distributive," or "procedural," or "substantive." Distributive justice is about a fair, if not equitable, distribution of burdens and benefits goods and evils, throughout society. Procedural justice has to do with contracts and with due process. If one is wronged, the wrong can be corrected or compensated for through due process. The assumption seems to be that monetary compensation can somehow "right" an injury. Substantive justice quantifies justice so that each person will

receive a level deemed by society to be adequate. In every case, justice is reduced to a commodity, or an entity which is subject to some kind of formula for allocation.

During the past 20 years the profession of medicine, medical ethicists, and philosophers of medicine have made the principle of autonomy, or self-determination, or individual rights, the basic value for decisions in health care. The courts have generally supported this in their opinions, usually on appeal, affecting the withdrawal or withholding of treatment.⁷ This seems to be the way that justice is served or done. It has also been argued that hospitals "must remain flexible enough to honor the competent wishes of their patients without forcing them to return home or engaging in 'ethical dumping' by transferring them to other institutions."⁸

I wish to suggest, and I ask you to consider, that as noble and well intentioned as is the emphasis on individual rights, this view is in keeping with the Enlightenment philosophy. It is a view that is inadequate for this postmodern era. It suggests that "anything goes" and reflects another failure of morality. The bottom line is not rights, self-determination or autonomy. We live in communities. We are members of families, churches and synagogues, neighborhoods, cities, states, a nation. As members of communities we have a claim on others, and others have a claim on us. Diogenes Allen uses a term from law to describe our value. He says we have "indefeasible value," value which cannot be annulled or undone.⁹ We have been made to participate in the life of community, and in the life of God. An exam-

ple of this kind of ethical justice is described in the biblical story of the good Samaritan.

... as noble and well intentioned as is the emphasis on individual rights, this view is ... inadequate for this postmodern era. It suggests that "anything goes" and reflects another failure of morality.

In this story, a man had been robbed, beaten, stripped and left for dead along the roadside. His condition was that he had no rights, no possessions, no social standing, no health insurance, no valid claims on any institution or anyone at all. In earthly terms, one could pass by without committing an act of injustice. There is no civil or legal obligation to stop and render aid. And the story says both a priest and a Levite passed by. It cannot be denied, however, that a just act is needed. One cannot let the cry of a human heart in distress go unanswered. It took a person from Samaria, a foreigner who happened along the way, to recognize this human plea for help and do something about it. The point is that moral goodness demands that we take others into account as a matter of justice. The issue of human need, whether for food, clothing, shelter, education, or health care is greater than all our concern about individual rights.

The ethical issues at the end of life are the same as the ethical issues at all stages of life. They are about life and death, the economy of the common-weal,

but, most importantly, they are rooted in our concept of justice as the exercise of our moral obligation to respond to others in their need.

References

- ¹ Allen, Diogenes, "Christian Values in a Post-Christian Context," in *Postmodern Theology*. Frederic B. Burnham, ed., Harper & Row, 1989, p. 21, ff.
- ² Callahan, Daniel, "The Limits of Medical Progress: A Principle of Symmetry," *The Center Report*, The Center for Public Policy and Contemporary Issues, Volume 2 Number 1, University of Denver, Winter/Spring, 1990.
- ³ Kitzhaber, Senator John, "Rationing Health Care: The Oregon Model," *Ibid*.
- ⁴ Meyer, Charles, "Eleven Myths about death," *The Witness*, March, 1987.
- ⁵ Vaux, Kenneth, "The Theologic Ethics of Euthanasia," *Hastings Center Report*, January/February 1989, Volume 19 Number 1, p. 20.
- ⁶ Vaux, Kenneth, *Ibid*, p. 22.
- ⁷ Annas, George J., "Transferring the Ethical Hot Potato," *Hastings Center Report*, February 1987, Volume 17 Number 1, pp 20 ff.
- ⁸ Annas, George J., *Ibid*.
- ⁹ Allen, Diogenes, *op. cit.* p. 29.

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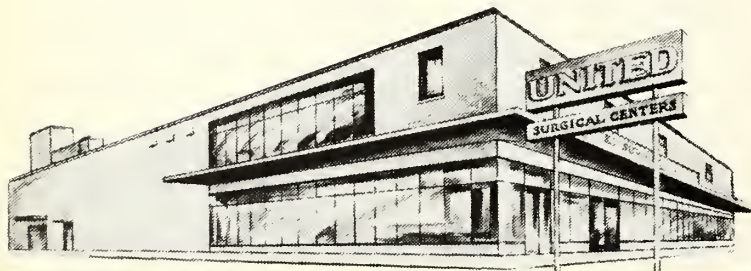
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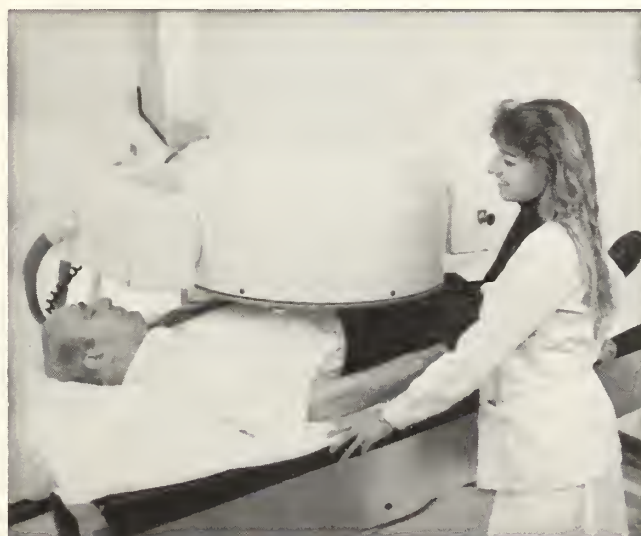
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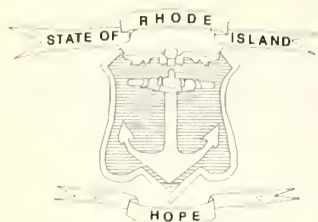
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Department of Health
H. Denman Scott, MD, MPH
Director of Health

Cesarean Section Rates in Rhode Island, 1986-1988

In 1965, 4.5% of births in the United States were delivered by cesarean section. By 1988, the proportion of deliveries by this method approached one-quarter. In Rhode Island, high C-section rates at some hospitals in the early 1980s led to the passage of R.I.G.L. 23-13-16.1 by the Rhode Island General Assembly, requiring each maternity hospital in the state to submit its C-section rate to the Director of Health annually, beginning with 1988 data. (All affected hospitals except one, with 4% of statewide deliveries, have also reported data for 1986 and 1987). These data are collected by the Office of Data and Evaluation of the Division of Family Health. This report presents the submitted data, supplemented by national data and data on vaginal births after a previous cesarean section (VBACs) from sources listed below.

In 1988, 75.8% of the 14,555 deliveries occurring in Rhode Island hospitals were vaginal deliveries where the mother had had no previous C-section, and 22.4% were C-sections (13.1% primary, 9.3% repeat) (Figure 1). The remaining 1.9% were VBACs; VBACs represented 17% of deliveries to women with previous C-sections, up from 14% in 1986.

Rhode Island's cesarean section rate in 1988 was more than 2 percentage points lower than the rate for the United States (24.7%), the result of contrasting trends in the two areas since 1986, when the rates were nearly identical (Figure 2). For each year since 1986, the Rhode Island rate has decreased while the US rate increased. Most of the decline in the Rhode Island rate is due to the decrease in the

primary C-section rate from 14.4% of all births in 1986 to 13.1% in 1988.

The rate of cesarean sections among individual hospitals in Rhode Island varied between 20.4% and 30.8% in 1988 (Figure 3). This spread has decreased since 1986 because of the decrease in the maximum rate observed each year. The statewide rate is driven primarily by the rate for Women and Infants Hospital, where over 60% of births in the state occur. Women and Infants' rate has fallen by more than 2 percentage points over the two-year period, from 23.1% to 20.9%. The hospital has maintained a C-section rate below the statewide rate in each year while serving as a referral center for high-risk births.

These recent data are a source of optimism that the upward spiral in cesarean section rates has been tempered locally and perhaps even reversed. Especially encouraging are the reduction in primary cesarean rates, which will in turn decrease the need for repeat C-sections in future years, and the slowly increasing VBAC rate. If these trends continue, the state can look forward to a period where the statewide cesarean section rate stabilizes and rates at the various hospitals exhibit less variation than has been the case in the past.

Data Sources:

National Center for Health Statistics, *Health United States 1989*, US Department of Health and Human Services, March 1990; DHHS Pub. No. (PHS) 90-1232.

Retsinas JM, *Cesarean Sections in Rhode Island Hospitals*, Rhode Island Health Policy and Planning Consortium, March 1990

Figure 1. Births in Rhode Island Hospitals by Type of Delivery, 1988.

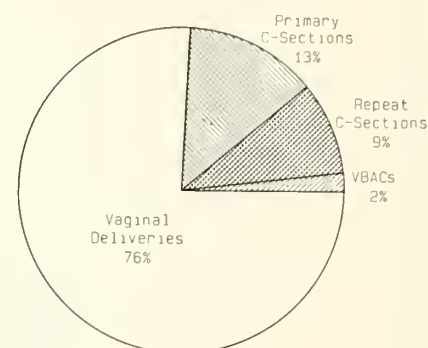


Figure 2. Cesarean Section Rate, Rhode Island and United States, 1986-1988.

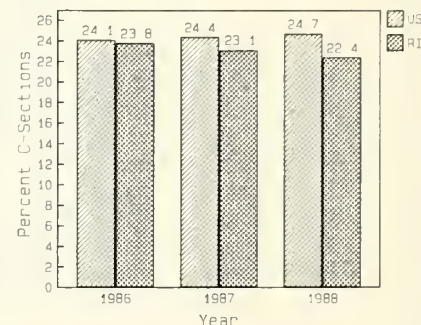
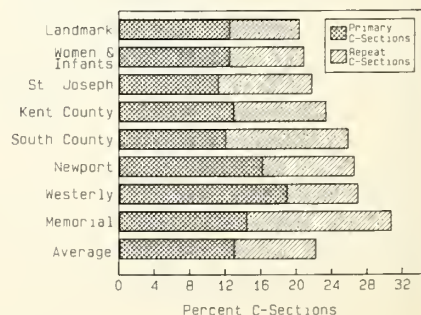


Figure 3. Cesarean Section Rates by Hospital, Rhode Island, 1988.



STATE OF RHODE ISLAND Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period		12 Months Ending with April 1990	
	April 1990			
	Number	Number		Rates
Live Births	1,362	15,753		15.9*
Deaths	810	9,729		9.8*
Infant deaths	(9)	(151)		9.6†
Neonatal deaths	(8)	(125)		7.9†
Marriages	504	8,165		8.2*
Divorces	241	3,712		3.7*
Induced Terminations	618	7,757		492.4†
Spontaneous Fetal Deaths	105	1,165		74.0†
Under 20 weeks' gestation	(100)	(1,063)		67.5†
20 +weeks' gestation	(5)	(95)		6.0†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period		12 Months Ending with January 1990		
	January 1990				
	Number (a)	Number (a)	Rates (b)	YPLL (c)	
Diseases of the Heart	328	3,442	346.6	4,223.0	
Malignant Neoplasms	214	2,432	244.9	6,493.5	
Cerebrovascular Diseases	55	597	60.1	852.0	
Injuries (Accident, Suicide, Homicide)	43	448	45.1	10,334.0	
COPD	35	324	32.6	450.0	

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 993,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

Rhode Island Medical Society



STATEWIDE PHYSICIAN GROUP PURCHASING PROGRAM for RIMS Members

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Based on national studies, the AMA estimates that the average solo practicing physician spends in excess of \$16,000 annually on office supplies and equipment. In the belief that Group Purchasing can accomplish significant savings for its members, The Rhode Island Medical Society, utilizing the experience and expertise of the Connecticut Health Institutional Services, Inc. (An affiliate of the Connecticut Hospital Association), identified areas of need and critically examined a number of companies.

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Hartford Office Supply Co., Inc.	Office Supplies
Henry Schein, Inc.	Medical Sales
Kenneth D. Margelot, Inc.	Computerized Medical Office/ Practice Management Systems Consulting Services
Moore Business Forms	Hospital Systems
Motorlease	Auto Leasing
Safeway Disposal Systems, Inc.	BioMedical Waste
Sears Business Centers	Computer Hardware/Software Equipment
Trans Union Medical Leasing Company	Equipment Leasing

RIMS Member Physicians interested in benefitting from group purchasing should contact Barbara Hicks at 331-3207.

THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME I
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (August, 1940)

C.P. Fitzpatrick, MD, Superintendent of the State Hospital in Howard, Rhode Island, writes the lead article on recent concepts of the convulsive disorders. The article describes a new instrument of investigation, the cathode ray oscillograph, "which will actually record the electrical potentials generated in various regions of the brain." The author summarizes some of the diagnostic advantages of electroencephalographic inquiry, noting in passing that Bradley Hospital in Providence was the first place in the United States where such clinical studies were conducted.

The second contribution is entitled "Delirium as a Danger Signal" and is written by Ira Nichols, MD of the Butler Hospital. The author defines delirium as an acute psychosis characterized by disorganization of the personality along the lines of confusion, illusion and the production of vivid and detailed hallucinations. These behavioral changes are characteristically accompanied by anxiety or panic, tachycardia, and restlessness. The author stresses that delirium, a grave danger

signal, must be distinguished from the manic-depressive, involuntional or schizophrenic psychoses. Nichols notes that many instances of delirium may be traced to the use of pharmacologically active agents particularly alcohol, bromides, morphine, and the barbiturates; nutritional deficiency diseases such as pellagra, dehydration and fecal impaction in the elderly are also indicted in the etiology of delirium.

This issue of the *Journal* carries a special article entitled, "Physicians Needed for Army Service." The qualifications for a commission into the Medical Corps are listed and the beginning salary for an unmarried first lieutenant is \$2,696 per year. (*Ed. Note: In August, 1940, the German armies control most of continental Europe; France has surrendered and the Russian armies are in retreat before the invading German divisions. England, in the west, stands alone although is now receiving military supplies from the United States, which is still at peace.*)

Through the kindness of Dr Halsey DeWolf, the *Journal* publishes an article on the early medical history of Kent County, Rhode Island. The article is a personal memoir written some indeterminate years ago by J. H.

Eldredge, MD, the president of the Rhode Island Medical Society in the year 1858. The author describes East Greenwich of the early nineteenth century, its local practitioners of medicine, and the therapies which they employed. The region, he notes, is singularly beautiful and essentially free of major illnesses except for epidemic influenza and the malignant fever "which raged so extensively all over New England in the year 1812 to 1814." The earliest recorded physician in this region was a Thomas Spencer, the seventh and youngest son "and according to custom was a doctor by birthright, educated as a physician, and the first who practiced medicine in this part of the state." His practice began about 1690 and continued until 1740. (Spencer, a member of the Society of Friends, was in later years a preacher as well.) Other early physicians in Kent County included Dr Dutee Jerauld whose parents were French Huguenot refugees. A Scottish physician Joseph Joslyn practiced from 1770 to 1780 in East Greenwich, dying after "giving himself up to the habits of intemperance." During the succeeding two years there were no physicians settled in the region until Dr Peter Turner, recently dis-

charged as an army surgeon with the Rhode Island Regiment, began a long, geographically extensive and illustrious practice in the Greenwich region. Turner, incidentally, served in the Continental Army at the Battle of Red Bank fighting against the Hessians.

The Rhode Island Medical Society Committee on Scientific Work reports that teaching clinics for its members will be conducted at Homeopathic, Providence Lying-In, Butler and Memorial Hospitals. The Charles V. Chapin Hospital announces its internship roster to include Drs I. Magnet, M. Burlingame, C. Eddy, O. Wermer, S. Smith, R. Rice, W. Crosby, and F. Lamb.

Twenty Five Years Ago (August, 1965)

The principal article concerns a five-year epidemiological survey of maternal mortality in Rhode Island and is written by Drs Stanley Davies and J. Kenneth Beezer, representing the Maternal Health Committee of the Rhode Island Medical Society. The authors define maternal death as a death of any patient who is pregnant or who expires within 90 days after the termination of her pregnancy. These deaths are considered in one of three categories: (1) direct obstetrical deaths, (2) indirect obstetrical deaths, and (3) non-related maternal deaths. Of a total of 92,258 live births in Rhode Island during the years 1960 through 1964, there were 41 maternal deaths of which 18 were direct obstetrical deaths, 11 were indirect obstetrical deaths and 12 nonrelated or unclassified. Amongst the direct

obstetrical deaths, 11 were due to hemorrhage, three to infection, one to eclampsia, one to pulmonary amniotic fluid embolism and two to anesthesia.

Amongst the indirect deaths, cardiac disease, pneumonitis, appendicitis and suicide were listed. The authors note that the maternal mortality rate (per 10,000 live births) was 1.27, the lowest of any of the states. The national rate for these years was 3.64. The authors further observe that the maternal mortality rate in Rhode Island, in 1930, was 78. They conclude, "There were no deaths from hemorrhage in the Group 1 hospitals where there was 24 hour coverage by an anesthesiologist." And, "... as long as our Maternal Health Committee is finding that there are avoidable factors in 59% of our maternal deaths, we still have an important task ahead."

Banice Webber, MD describes the hypercalcemic syndrome which is a frequent complication during the course of advanced breast cancer with metastases to bone. The syndrome should be considered when a breast cancer patient develops polyuria, polydipsia, nausea, vomiting or lethargy. The syndrome can be controlled by simple therapeutic measures.

Drs Ray Lundgren, Jr, Robert Kugel and Francis Corrigan summarize the seven cases of phenylketonuria detected in Rhode Island during the first year of mass statewide screening with the Guthrie test. These seven cases were detected in about 19,000 newborns. The article demonstrates the immense financial and emotional benefits realized by means of this mass-screening.

The actions of the House of Delegates of the American Med-

ical Association (meeting of June, 1965) are summarized by Drs Arthur Hardy and Edmund Hackman. The most controversial issue considered was that of "non-participation under any so-called "Medicare" law that might be passed by Congress." The House recommended that "the members of the American Medical Association be reminded that it is each individual physician's obligation to decide for himself whether the conditions of a case for which he is about to accept responsibility permit him to provide his own highest quality of medical care." The House of Delegates also reaffirm nine principles for maintaining high standards of health care programs. These principles include the following: "No person needing health care shall be denied such care because of the inability to pay for it." and, "It is appropriate that government revenues be used to finance health care when other resources have been found to be inadequate." In an effort to reconcile differences, the House of Delegates offers to meet with President L. Johnson "with a view to safeguarding the continued provision of the highest quality and availability of medical care to the people of the United States."

Arcieri's third edition of *Benjamin Franklin in Medicine* is reviewed by Dr Ronchese. We are reminded of Franklin's genius in many fields of endeavor, including his seminal studies on contagion, gout, small-pox, lead poisoning, mesmerism and even the design of urethral catheters.

[Ed. Note: The John Carter Brown Library at Brown University houses one of the finest collections of Frankliniana in the United States.]



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Hypotension: Excessive hypotension is rare in uncomplicated hypertensive patients treated with VASOTEC alone. Patients with heart failure given VASOTEC commonly have some reduction in blood pressure, especially with the first dose, but discontinuation of therapy for continuing symptomatic hypotension usually is not necessary when dosing instructions are followed; caution should be observed when initiating therapy. (See DOSAGE AND ADMINISTRATION.) Patients at risk for excessive hypotension, sometimes associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death, include those with the following conditions or characteristics: heart failure, hypotension, high-dose diuretic therapy, recent intensive diuresis or increase in diuretic dose, renal dialysis, or severe volume and/or salt depletion of any etiology. It may be advisable to eliminate the diuretic (except in patients with heart failure), reduce the diuretic dose, or increase salt intake cautiously before initiating therapy with VASOTEC in patients at risk for excessive hypotension who are able to tolerate such adjustments. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients at risk for excessive hypotension, therapy should be started under very close medical supervision and such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart disease or cardiovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of VASOTEC, which usually can be given without difficulty once the blood pressure has stabilized. If symptomatic hypotension develops, a dose reduction or discontinuation of VASOTEC or concomitant diuretic may be necessary.

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: **General Impaired Renal Function:** As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta-adrenergic-blocking agents, methyldopa, nitrates, calcium-channel blocking agents, hydralazine, prazosin, and digoxin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no teratogenicity or fetotoxicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radioactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not

been clearly defined, VASOTEC[®] (Enalapril Maleate, MSD) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome: Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypotension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of ¹⁴C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2987 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were: headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were: dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were: fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), angina pectoris (1.5%), nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring since the drug was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients (see WARNINGS, Hypotension), pulmonary embolism and infarction, pulmonary edema, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis (hepatocellular or cholestatic jaundice), melena, anorexia, dyspepsia, constipation, glossitis, stomatitis, dry mouth.

Musculoskeletal: Muscle cramps.

Nervous/PSYCHIC: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Respiratory: Bronchospasm, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, anosmia, tinnitus, conjunctivitis, dry eyes, tearing.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgias/arthritis, myalgias, fever, serositis, vasculitis, leukopenia, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 1% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: Hypertension: In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed.

If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium (see PRECAUTIONS).

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance >30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 2.5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure who have hyponatremia (serum sodium <130 mEq/L) or with serum creatinine >1.5 mg/dL, therapy should be initiated with 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d., then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more, if at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function. The maximum daily dose is 40 mg.

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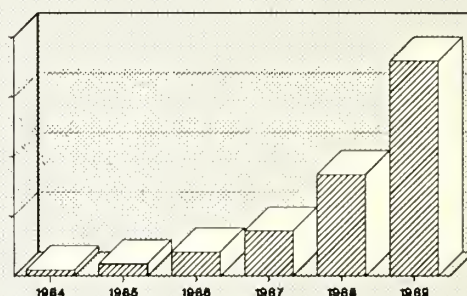


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Cover: "The Anatomy Lesson," a painting by Thomas de
Keyser (1596-1667), a portrait artist from Amsterdam.

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EDITORIALS

Medical Education in Rhode Island, 1990

The three components of formal medical education — undergraduate, graduate and continuing — have expanded substantially in Rhode Island during the last few decades.

Residency training programs, now called graduate medical education programs, had been long established in regional hospitals, notably Rhode Island Hospital, but it wasn't until 1962 that efforts during this century were begun in undergraduate medical education. In that year, Brown University established a master's degree in medical science, equivalent in educational content to the two basic science years of the conventional medical curriculum. In 1972, with the active cooperation of eight community hospitals, this program was expanded to a four year MD - conferring effort which was promptly approved by the Liaison Committee on Medical Education, at that time, the national agency for the accreditation of United States medical schools. The inaugural class of 58 physicians was graduated in June, 1975. Fifteen subsequent classes have now been awarded medical degrees by Brown, generating a total of 1,094 physicians. Many recent graduates are still in residency training or in the armed services, but 113 of these physicians have already established medical practices in Rhode Island; and it is estimated, by the year 2000, that Brown will have provided more physicians to this community than any other medical school.

In this issue of the *Journal*, Dr Stephen R. Smith, Associate Dean of Medicine at Brown, summa-

rizes the backgrounds and residency training commitments of the 80 men and women who had received their MD degrees from Brown this past May, 1990.

There are, currently, 127 accredited medical schools in mainland United States and the Commonwealth of Puerto Rico, educating 65,150 medical students and graduating this past year some 15,646 physicians. Seventy-six (59.8%) of the 127 schools are public-owned or managed. With the exception of Brown, no new private medical school has been opened in New England since 1893. Indeed, of the 47 US medical schools established since 1945, 36 (77.0%) are public entities. Of the 11 private schools, three are church-sponsored and two (Mayo and Mt Sinai) are educational outgrowths of previously established clinical centers.

Six of New England's nine medical schools were established prior to this century. The medical school at Brown is the youngest of these nine institutions (although Brown had operated a small medical school in 1811 — the faculty consisting of Profes-

sors Solomon Drowne, William Ingalls and William C. Bowen — and had graduated 87 physicians until 1832 when the school was "temporarily closed.")

How well do present students, declaring Rhode Island as their home, fare in achieving acceptance to these 127 approved medical schools? Not quite as well as the national mean. In the United States, there now are about 6.5 medical school acceptances per 100,000 population per year; for Rhode Island, the number is 5.0 (ie, 49 acceptances per 986,000 population).

To what extent are the private medical schools of New England sensitive to the educational needs of their instate applicants? Brown seems to do somewhat better than most private medical schools of this region.

The second component of medical education, residency training, has also developed significantly in Rhode Island during these past three decades. Approved residency training programs in virtually every specialty are now offered by many of the hospitals of this state. There are 43 training programs in the state,

The Medical Schools of New England			
Name	Year Established	Ownership	Student Body
Harvard	1782	private	646
Dartmouth	1797	private	301
Yale	1812	private	462
Vermont	1822	public	370
Boston	1873	private	608
Tufts	1893	private	612
Connecticut	1961	public	350
Massachusetts	1962	public	407
Brown	1972	private	289

with 379 resident physicians. Some of these residency programs have been consolidated under medical school supervision, thus offering the trainee the advantages of a multi-institutional education. An article by Dr F. Schiffman, in this issue of the *Journal*, describes these graduate medical education programs in greater detail.

Private New England Medical Schools Percent of Class Made Up of Instate Students	
School	Instate Students (%)
Boston	33.3%
Brown	31.1%
Dartmouth	9.9%
Harvard	10.5%
Tufts	22.2%
Yale	6.9%

The Residency Training Programs of New England		
State	No. Programs	No. Resident Physicians
Connecticut	132	1,574
Maine	15	172
Massachusetts	277	3,399
New Hampshire	21	188
Rhode Island	43	379
Vermont	25	165

The high professional capabilities of the current house staffs in the hospitals of Rhode Island are reflected in the scientific contributions which many resident physicians have made during the Spring, 1990 Annual Scientific Meeting of the Rhode Island Chapter of the American College of Physicians. Abstracts of 19 of these contributions are also included in this issue of the *Journal*.

The *Rhode Island Medical Journal* plans to publish annual summary information describing Brown's medical graduates, the resident physicians of our hospitals as well as updated demographic information about the practicing physicians of Rhode Island.

Stanley M. Aronson, MD

Guide to Clinical Preventive Services

1989 was a banner year for the advancement of preventive medicine. In 1989 the US Preventive Services Task Force published its *Guide to Clinical Preventive Services* (Williams & Wilkins Publishers). This is truly a landmark document. The Guide is the culmination of 4 years of intensive work by a highly competent 20 member Task Force and over 300 expert reviewers.

The Guide covers *screening* for vascular, neoplastic, metabolic, infectious diseases, hematologic, ophthalmologic, otologic, prenatal, musculoskeletal, mental disorders, and substance abuse. It also includes *counseling* for tobacco, exercise, nutrition, safety belts, injuries, HIV, sexually transmitted diseases, unintended pregnancy, and dental disease. In addition, the Guide addresses *immunizations/chemoprophylaxis*:

childhood and adult immunizations, and postexposure, estrogen and aspirin prophylaxis. In all there are 60 different illnesses/conditions and an assessment of the effectiveness of 169 interventions covered in the Guide. All physicians will not agree with each recommendation. However, on most there is wide consensus.

As Director of Health, I am sufficiently impressed with this document that I believe all physicians with major primary care responsibilities should have a copy in their offices. While the single copy is \$20, the Department of Health with a bulk purchase obtained \$10 per copy purchase price. Thus far we have distributed some 1,500 copies to family physicians, internists, obstetricians, and pediatricians. All residents in training have also received a copy. The Department

will be happy to provide any physician with a copy as long as our current supply lasts. If you desire a copy, please call or drop me a note.

Finally, the Department of Health in cooperation with the *Rhode Island Medical Journal* is pleased to reprint the eight age-specific periodic health examination charts, which appear in the Guide. We urge that you save these eight pages so that they may be readily available for review. The interventions listed in these charts are not exhaustive. You should refer to appropriate chapters in the Guide for more detailed advice.

H. Denman Scott, MD
Director of Health



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References

- 1 *USP DI Update*, September/October 1988, p 120
- 2 *Br J Clin Pharmacol* 1985;20 710-713
- 3 *Data on file*, Lilly Research Laboratories
- 4 *Scand J Gastroenterol* 1987;22(suppl 136) 61-70
- 5 *Am J Gastroenterol* 1989;84 769-774

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Precautions: General—1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests—False-positive tests for urobilinogen with Multistix[®] may occur during therapy.

Drug Interactions—No interactions have been observed with theophylline, chloridiazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A two-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a two-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given

an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a two-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect, but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in one fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in one fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions. Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events was due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to three times the upper limit of normal, however, did not significantly differ from that in placebo patients. Hepatitis and jaundice have been reported. All abnormalities were reversible after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered Axid and in three untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumentary—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage—Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for four to six hours increased plasma clearance by approximately 84%.

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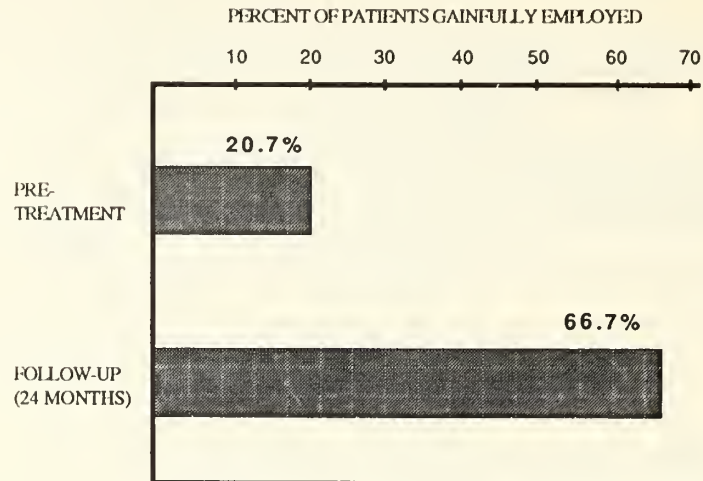
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The Brown University Program in Medicine Class of 1990

Stephen R. Smith, MD

The purpose of this article is to introduce the graduates of the MD Class of 1990 to the physician community of Rhode Island . . .

Eighty men and women received the Doctor of Medicine degree from Brown University on May 28, 1990, representing the fifteenth class of physicians graduated from that institution in this century. If this class follows the pattern of preceding classes, approximately 11% will eventually enter the practice of medicine in the State of Rhode Island. Of the 1,014 physician graduates of previous classes, 113 are currently practicing in Rhode Island.

The purpose of this article is to introduce the graduates of the MD Class of 1990 to the physician community in Rhode Island, since many will be your future professional colleagues.

A Portrait of the Class of '90

The 80 graduates are nearly equally divided between the sexes, with 55% being men, and 45% women. This is a pattern that has characterized the graduates of the Brown medical school for the past decade.

The racial composition of the class, as shown in Table 1, shows

Stephen R. Smith, MD, is Associate Dean of Medicine and Professor of Family Medicine with the Brown University Program in Medicine, Providence, Rhode Island.

considerable diversity, with more than one-quarter of the class belonging to minority groups. Students from an Asian background represent the most rapidly growing ethnic group in the medical school over the last few years. This trend is likely to continue based on admission data to the eight-year Program in Liberal Medical Education (PLME) through which most future graduates will come.

Slightly more than one-quarter of the class are residents of Rhode Island. This percentage has been stable over the past decade and is likely to remain so. The two international students hail from Greece and Pakistan. The number of foreign students is likely to gradually increase as the PLME has gained international prominence in recent years.

Among Rhode Island high schools, Moses Brown provided the most students to the Class of 1990 with four students having been graduated from there. Two students each were graduates of Bishop Stang, Classical, and Toll Gate high schools. Outside of Rhode Island, Stuyvesant High School in New York City was the leader with three graduates having attended that highly-selective secondary school.

Almost half of the class (37

graduates) came through the combined AB-MD program at Brown known as the Medical Education Program (MEP). The MEP is the seven-year predecessor of the PLME. Students are admitted to the MEP directly from high school and pursue a seven-to-eight year continuum of liberal arts and medical education. Traditionally-admitted students from four-year undergraduate premedical programs accounted for another one-quarter of the class. Another 18 students (22.5 percent) were members of the Brown/Dartmouth Medical Program in which the students spend their first two years of medical school at Dartmouth before completing their last two years at Brown. The remainder of the class was composed of four students who transferred from other medical schools and one student who was part of the MD/PhD program.

Not surprisingly, Brown University was, by far, the most common undergraduate college among the graduates. Nearly half the class (39 students) were Brown graduates. Dartmouth Col-

ABBREVIATIONS USED:

MEP: Medical Education Program

PLME: Program in Liberal Medical Education

lege ranked second with seven members of the Class of 1990 having that school as their alma mater. Stanford University was the third most common undergraduate college with four graduates among the class. Altogether, the graduates of the Class of 1990 came from 29 different colleges and universities.

While internal medicine remains the most frequently selected specialty, the proportion of the graduates entering internal medicine continues to shrink. This is consistent with a national trend away from internal medicine and toward the surgical subspecialties and institutional specialties such as anesthesiology and radiology.

The most common undergraduate major among the class members was biology, with exactly half the class selecting that as their undergraduate field of study. Eighty percent of the class were science majors, while 5% majored in the social sciences and 15% majored in the humanities. Among the social science majors, economics was the most common choice, while history was the most common choice among those majoring in the humanities.

Where They Are Going

While internal medicine remains the most frequently selected specialty, the proportion of the graduates entering internal medicine continues to shrink, as shown in Table 2. This is consistent with a national trend away from internal medicine and toward the surgical subspecialties and institutional specialties such as anesthesiology and radiology.

The proportion of the class entering specialties in primary care rose from the previous year, though the four-year trend is still downward. Increases in the number of graduates going into pediatrics and family practice compensated for the decline in internal medicine. Figure 1 illustrates the specialty choices of the Class of 1990.

Table 3 lists all of the Class of 1990 graduates and where they will be going to do their residency training. Of the 77 graduates who will enter residency training next year (3 are delaying their residencies for 1 year), 16 graduates (21%) matched with Brown-affiliated residency programs and will be staying in the state. Next to Providence, New Haven seemed to be a particularly attractive place for the Class of 1990, with six of its members going to the Yale-New Haven Hospital for their first year of residency training.

California and New York each will be the home for 13 graduates next year and rank second to Rhode Island (16) as the most popular states for residency training.

California and New York each will be the home for 13 graduates next year and rank second to Rhode Island (16) as the most popular states for residency training. Table 4 lists those states where the graduates will be going for their first year of residency training. As with preceding classes, this class overwhelmingly preferred the Northeast and West Coast to the South and Central states. Over two-thirds (67.5%) will be spending their first year of residency in the Northeast and nearly one-fifth (18.2%) on the West Coast. In contrast, only

five students (6.5%) will be in the South (including Texas), and six students (7.8%) will be in the Central region.

Conclusion

The Brown University Program in Medicine MD Class of 1990 reflects national trends in specialty choice. Whether this trend away from primary care specialties is reversed as the Resource-Based Relative Value Scale changes the balance in physician income remains to be seen. The increase in the proportion of graduates in the Class of 1990 going into primary care specialties may be the first point on a new, upward deflection of the curve, or it may simply be a "blip" on the downward trend observed over the last few years.

Acknowledgements

My thanks to Ruth Sauber and Linda Collette in the Office of Medical Student Affairs, Brown University Program in Medicine for assistance in summarizing the data. Thanks, too, to Hank Randall for the class photograph.

Address correspondence to: Stephen R. Smith, MD, Box G-A218, Brown University Program in Medicine, Providence, RI 02912 (401) 863-2894.

Table 1. Demographic Characteristics of the MD Graduates of the Brown University Program in Medicine Class of 1990

	No.	Percent
Sex		
Male	44	55.0
Female	36	45.0
Race		
White	58	72.50
Asian	12	15.00
Black	5	6.25
Mexican-American	2	2.50
Portuguese-American	2	2.50
Other Hispanic	1	1.25
State of Residence		
Rhode Island	21	26.25
New York	15	18.75
California	10	12.50
Massachusetts	8	10.00
Illinois	4	5.00
Connecticut	3	3.75
Maryland	3	3.75
New Jersey	3	3.75
Other States	11	13.75
Other Countries	2	2.50

Figure 1. Specialty choices of the Brown University Program in Medicine Class of 1990.

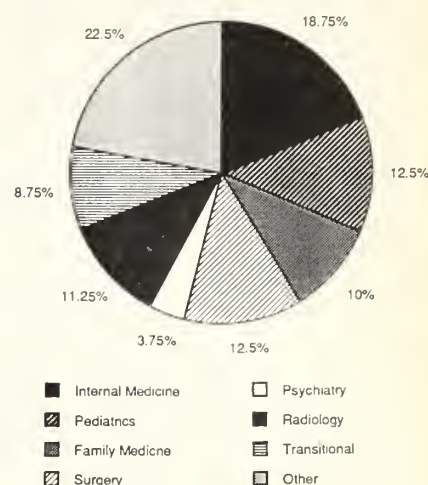


Table 2. Specialty Choices of the MD Graduates of the Brown University Program in Medicine Class of 1990

Specialty Choice	Graduating Class							
	No.	1987 (%)	No.	1988 (%)	No.	1989 (%)	No.	1990 (%)
Internal Medicine, total	23	(30.3)	22	(27.8)	20	(25.0)	15	(19.5)
Categorical Medicine	23	(30.3)	19	(24.0)	14	(17.5)	13	(16.9)
Primary Care Medicine	0	(0.0)	3	(3.8)	6	(7.5)	2	(2.6)
Pediatrics	11	(14.7)	10	(12.7)	7	(8.8)	10	(13.0)
Family Medicine	5	(6.7)	6	(7.6)	4	(5.0)	8	(10.4)
Medicine/Pediatrics	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.3)
Total Primary Care	40	(53.3)	38	(48.1)	31	(38.8)	34	(44.2)
Surgery	9	(12.0)	9	(11.4)	6	(7.5)	10	(13.0)
Surgical Subspecialties	5	(6.7)	2	(2.5)	15	(18.8)	4	(5.2)
Ophthalmology	2	(2.7)	2	(2.5)	6	(7.5)	3	(3.9)
Orthopedics	1	(1.3)	0	(0.0)	4	(5.0)	0	(0.0)
Neurosurgery	0	(0.0)	0	(0.0)	2	(2.5)	0	(0.0)
Urology	1	(1.3)	0	(0.0)	1	(1.3)	0	(0.0)
Plastic Surgery	0	(0.0)	0	(0.0)	1	(1.3)	0	(0.0)
Otorhinolaryngology	1	(1.3)	0	(0.0)	1	(1.3)	1	(1.3)
Emergency Medicine	0	(0.0)	2	(2.5)	2	(2.5)	1	(1.3)
Obstetrics & Gynecology	3	(4.0)	4	(5.1)	7	(8.8)	4	(5.2)
Psychiatry	6	(8.0)	4	(5.1)	5	(6.3)	3	(3.9)
Neurology	3	(4.0)	4	(5.1)	3	(3.8)	1	(1.3)
Transitional	2	(2.7)	10	(12.7)	2	(2.5)	7	(9.1)
Institutional Specialties	7	(9.3)	6	(7.6)	9	(11.3)	13	(16.9)
Anesthesiology	4	(5.3)	2	(2.5)	4	(5.0)	3	(3.9)
Pathology	1	(1.3)	1	(1.3)	1	(1.3)	0	(0.0)
Rehabilitation Medicine	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.3)
Radiology	2	(2.7)	3	(3.8)	4	(5.0)	9	(11.7)
Totals*	75	(99.7)	79	(100.1)	80	(100.3)	77	(100.1)

*Totals do not add to 100.0 due to rounding

Table 3. Brown University Program in Medicine Class of 1990 Residency Positions

Name of Graduate	Hospital Name/Med. School Affiliation	Specialty
Anawis, Monique	Miriam Hospital/Brown University	Internal Med/Prelim
Ang, David	Affiliated Hospitals/University of Rochester	Ophthalmology
Ankenbrandt, William	San Fernando Valley/U-Calif Los Angeles	Internal Medicine
	Ravenswood Hospital/University of Illinois	Transitional
Armstrong, Mary	McGaw Medical Center/Northwestern University	Diag. Radiology
Arreola, Rodolfo	Coordinated Programs/Univ. of Massachusetts	Surgery
Ashley, Michelle	Affiliated Hospitals/Marshall University (Huntington, WV)	Surgery-Prelim.
Baker, Lisa	Memorial Hospital/Brown University	Family Medicine
Baum, Sarah	Delaying residency	
Baziotis, Peter	Yale-New Haven Hospital/Yale University	Pediatrics
	Yale-New Haven Hospital/Yale University	Internal Medicine/Prelim
	Yale-New Haven Hospital/Yale University	Anesthesiology
Becker, Jeffrey	North Shore Univ. Hospital/Cornell University	Internal Medicine/Prelim
	Yale-New Haven Hospital/Yale University	Radiology
Bell, Lynn	Delaying residency	
Benedetti, Fabio	Strong Memorial Hospital/Univ. of Rochester	Internal Medicine
Benoit, Debbie	Rhode Island Hospital/Brown University	Pediatrics
Bilodeau, Elise	G.W. University Hospital/George Wash. Univ.	Internal Medicine-Prelim
Breuer, Christopher	Rhode Island Hospital/Brown University	Surgery
Butcher, Robert	Scott AFB Regional Hospital/Scott AFB, Ill.	Family Medicine
Carcieri, David	New York Hospital/Cornell University	Ob/Gyn
Carpenter, Todd	Affiliated Hospitals/University of Chicago	Medicine/Pediatrics
Chang, Ophelia	Affiliated Hospitals/Tufts University	Ob/Gyn
Chang, Yuan-Fei	Harbor UCLA Med. Ctr./U-Calif Los Angeles	Family Medicine
Chapdelaine, Jeffrey	New England Deaconess/Harvard University	Surgery/Prelim
Cheever, Laura	Affiliated Hospitals/U-Calif-San Francisco	Internal Medicine
Chen, Anthony	County Medical Center/Univ. of So. California	Internal Medicine
Cheng, Helen	Rhode Island Hospital/Brown University	Internal Med-Primary
Chidekel, Aaron	Yale-New Haven/Yale University	Pediatrics
Chiu, Christopher	San Joaquin General Hospital/U-Calif Davis	Family Medicine
Colliton, Julie	Coordinated Programs/Univ of Massachusetts	Surgery
Davy, Charmaine	Roger Williams Hospital/Brown University	Internal Med
Deluca, Bethanne	Rhode Island Hospital/Brown University	Pediatrics
Deutsch, Jason	Miriam Hospital/Brown University	Transitional
	Affiliated Hospitals/Emory University	Diag. Radiology
Driscoll, Daniel	Massachusetts General Hospital/Harvard University	Surgery
Friedberg, Karen	Miriam Hospital/Brown University	Internal Medicine/Prelim
	Rhode Island Hospital/Brown University	Neurology
Furey, Patricia	Hartford Hospital/University of Connecticut	Surgery
Geddes, Lauren	Rhode Island Hospital/Brown University	Pediatrics
Ginsberg, David	NYU Medical Center/New York University	Psychiatry
Greenwald, Corey	Roosevelt Hospital/Columbia University	Internal Med/Prelim
Harvey, Gwyn	Delaying residency	
Hohmann, Kirsten	Walter Reed (Bethesda)/Army	Internal Medicine
Hu, Linden	St. Elizabeth's Hospital/Tufts University	Internal Medicine
Hull, Meredith	Yale-New Haven/Yale University	Pediatrics
Husain, Syed	Affiliated Hospitals/Baylor College of Medicine	Transitional
	Affiliated Hospitals/Baylor College of Medicine	Ophthalmology
Imam, Naniyer	Combined Program/Univ. of South Florida	Diag. Radiology
Ip, Tze Kin	Western Penn. Hospital/University of Pittsburgh	Surgery
Johnson, Yeva	Affiliated Hospitals/U-Calif	Family Medicine
	San Francisco	
Kadish, Karen	Presbyterian Hospital/Columbia University	Psychiatry
Karp, Debra	Yale-New Haven Hospital/Yale University	Internal Med/Prelim
Katz, David	Georgetown Univ. Hospital/Georgetown University	Pediatrics
Kilmarx, Peter	Johns Hopkins Hospital/Johns Hopkins University	Internal Medicine
Kimmel, Stephen	Harbor-UCLA Medical Center/U-Calif Los Angeles	Transitional
Lefrancois, Darlene	St. Elizabeth's/Tufts University	Internal Medicine-Primary
Lemberg, Paul	Affiliated Hospitals/Northwestern University	ENT
Limp, Kevin	Duke University Med. Ctr/Duke University	Pediatrics/
	Johns Hopkins Hospital/Johns Hopkins University	Anesthesiology
Little, Virginia	Affiliated Hospitals/U-Calif, San Francisco	Surgery

Martins, Eduina	Georgetown Hospital/Georgetown University	Psychiatry
McGrath, Carolyn	Rhode Island Hospital/Brown University	Internal Medicine
Medellin, Roland	John Peter Smith Hosp/U-Texas SW Med. School	Family Medicine
Mendes, Manuela	Memorial Hospital/Brown University	Family Medicine
Mungovan, John	Miriam Hospital/Brown University	Internal Med/Prelim
	Rhode Island Hospital/Brown University	Radiology
Murphy, John	Temple University Hospital/Temple University	Internal Medicine
Nanevicz, Tania	Mt. Sinai Hospital/Mt. Sinai School of Medicine	Internal Medicine
O'Dea, Catherine	Children's Hospital/University of Pennsylvania	Pediatrics
Ouano, Dean	Miriam Hospital/Brown University	Internal Med/Prelim
	Scheie Eye Institute/University of Pennsylvania	Ophthalmology
Pappas, John	Hartford Hospital/University of Connecticut	Ob/Gyn
Porro, Julio	Community Hospital/U. Calif, San Francisco	Family Medicine
Prescott, Jon	Cleveland Clinic Fdn/Case Western Reserve	Radiation Oncology
Robinson, Terry	Affiliated Hospitals/Stanford University	Pediatrics
Ross, Andrew	Cambridge Hospital/Harvard Medical School	Transitional
Royer, Elizabeth	Miriam Hospital/Brown University	Internal Med/Prelim
	Cedars-Sinai Med Ctr/U. Calif Los Angeles	Diag Radiology
Salessiotis, Anatassios	Valley Medical Center/U. Calif San Francisco	Transitional
Schaffir, Jonathan	Mt. Sinai Hospital/Mt. Sinai School of Medicine	Ob/Gyn
Segall, Michelle	Staten Island Univ. Hosp/SUNY-Brooklyn	Internal Med/Prelim
	Bronx Municipal Hosp/Einstein Coll. of Medicine	Diag. Radiology
Sherman, John	Sparrow Hospital/Michigan State University	Emergency Medicine
Skipitaris, Nicholas	NYU Medical Center/New York University	Internal Medicine
Stafford, Debra	King-Drew Medical Center/U. Calif Los Angeles	Surgery
Treff, Elise	San Diego Naval Hospital/Navy	Surgery
Turchetta, John	Affiliated Hospitals/University of Washington,	Physical & Rehab Med
Umlas, Shari-Lyn	New York Hospital/Cornell University	Internal Med/Prelim
	New York Hospital/Cornell University	Diag. Radiology
Weisberg, Ronald	North Shore Univ. Hospital/Cornell University	Internal Med/Prelim
	University Hospital/University of Pennsylvania	Anesthesiology
Wirth, William	Rhode Island Hospital/Brown University	Pediatrics
Yank, Otto	NYU Medical Center/New York University	Internal Medicine

Table 4. State in Which the First Year of Residency Training is Located for the Brown University Program in Medicine MD Class of 1990

State	No.	(%)
California	13	(16.9)
Connecticut	7	(9.1)
District of Columbia	4	(5.2)
Florida	1	(1.3)
Illinois	4	(5.2)
Maryland	1	(1.3)
Massachusetts	8	(10.4)
Michigan	1	(1.3)
New York	13	(16.9)
North Carolina	1	(1.3)
Ohio	1	(1.3)
Pennsylvania	3	(3.9)
Rhode Island	16	(20.8)
Texas	2	(2.6)
Washington	1	(1.3)
West Virginia	1	(1.3)
Total*	77	(100.1)

*Total does not equal 100 due to rounding



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Graduate Medical Education at the Brown University Affiliated Hospitals and Institutions

Fred J. Schiffman, MD

Graduate medical education is a thriving enterprise in Rhode Island. Resident physicians and fellows now number almost 400 training within 18 approved Brown University-affiliated programs and 25 approved Brown University-affiliated fellowship programs (see tables 1 and 2).

Residency Programs

Allergy and Immunology: This is an accredited 2 year training program codirected by Donald Klein, MD and Guy Settupane, MD. Trainees are required to have completed a 3 year program in internal medicine or pediatrics. Training includes instruction in the basic sciences and trainees are encouraged to undertake research work.

Dermatology: The residency program in dermatology is directed by Charles J. McDonald, MD and is based at Memorial Hospital of Rhode Island, Rhode Island Hospital, Roger Williams General Hospital and the VA Medical Center. Off-campus locations for additional training include the Providence Health Centers, Inc., and the state-sponsored facility for the treatment of sexually transmitted diseases at St. Joseph Hos-

pital. Applicants to this training program are urged to complete prior residency training in internal medicine or pediatrics. The clinical faculty in dermatology numbers 25. Most graduates of this program enter clinical practice.

Family Medicine: This accredited 3 year program, directed by Alica Monroe, MD, stresses clinical competence, continuity of training and comprehensiveness for its 12 resident physicians. Graduates of the program enter a variety of practice settings ranging from solo urban practice to rural Health Maintenance Organizations, to family medicine in an academic setting. The program is based at Memorial Hospital and its affiliated Family Care Center. Residents also rotate through other Brown-affiliated hospitals, Lowell General Hospital and the private offices of certain local practitioners.

Internal Medicine: Brown's Department of Medicine, headed by Paul Calabresi, MD, sponsors several hospital-based accredited residency training programs which are currently interdependent and cooperative but not yet fully integrated. There are now over 180 residents in internal medicine who are based variously at Memorial Hospital of Rhode Island, Rhode Island Hospital, Roger Williams General Hospital and The Miriam Hospital. Each of these residents will

also rotate through the VA Medical Center. Currently, residents may select any of the aforementioned hospitals' satellite clinics, HMOs or private physicians' offices for elective experience. Efforts are underway to further integrate the ambulatory and inpatient components of the residency training program.

Greater attention is now invested in creating opportunities for all medicine residents in the Brown-affiliated hospitals to have access to the entire Department of Medicine faculty and to interact with other residents in the training program. An inter-hospital Medicine Residency Committee and the Council of Chiefs of Medicine meet regularly and provide a forum for discussion of items of mutual interest. Integrated activities now include

ABBREVIATIONS USED:

BH: Butler Hospital

EPBH: Emma P. Bradley Hospital

MHRI: Memorial Hospital of Rhode Island

OME: Office of Medical Examiner

RIH: Rhode Island Hospital

RWGH: Roger Williams General Hospital

TMH: The Miriam Hospital

VAMC: Veterans Administration Medical Center

WIH: Women and Infants Hospital

Fred J. Schiffman, MD, is Associate Physician in Chief at Brown University and Associate Director of Medicine at The Miriam Hospital, Providence, Rhode Island.

Medical Grand Rounds, A Resident Physicians' Research Day in conjunction with the American College of Physicians (see elsewhere in this issue), Brown Medical Students' Career Night, and Ethics Rounds in collaboration with Professors Edward N. Beiser and Dan Brock.

Many residents elect to obtain additional training in subspecialty disciplines and do so in Brown University-sponsored fellowships (see table 2) or at other accredited programs elsewhere in the United States. A surprisingly high number of former Brown resident physicians, who have sought further training elsewhere, choose to return to Rhode Island for careers in clinical practice or academic medicine.

An independent residency in general internal medicine is based at Rhode Island Hospital under the direction of Steven Wartman, MD. This program offers a comprehensive ambulatory experience and uses a multidisciplinary faculty to integrate the social and behavioral sciences into the fabric of post-graduate medical education.

Neurology: The training program in neurology, directed by J. Donald Easton, MD, is relatively new to the Brown residency system. There are nine residents in this accredited 3 year sequence. Most neurology residents have had up to 3 prior years of residency training in internal medicine. Their primary site of training is Rhode Island Hospital. Third Year residents rotate through Roger Williams General Hospital where they also participate in a movement disorders clinic.

The program graduated its first resident in June of 1990. This resident elected to remain at Brown for 2 further years as a fellow investigating the physiology of motor control.

The neurology training pro-

Table 1. Brown University Affiliated Residency Programs

Residency Program	Program Director	Principal Training Site
Allergy & Immunology	Donald Klein, MD	RIH
Child Psychiatry	Guy Settipane, MD	RIH
Dermatology	Charles Malone, MD	EPBH
	Charles McDonald, MD	RWGH, MHRI, RIH, VAMC
Diagnostic Radiology	Daniel Hanson, MD	RIH
	John Cronan, MD	
Family Practice	Alicia Monroe, MD	MHRI
	Patrick Dowling, MD	
Forensic Pathology	William Sturner, MD	OME
	Kristin Sweeney, MD	
General Internal Medicine	Steven Wartman, MD	RIH
Internal Medicine	Fred Schiffman, MD	TMH
Internal Medicine	Bryson Ley, MD	MHRI, VAMC
Internal Medicine	Al Most, MD	RIH
Internal Medicine	Paul Calabresi, MD	RWGH, VAMC
	Alan Weitberg, MD	
Neurosurgery	Mel Epstein, MD	RIH
Neurology	J. Donald Easton, MD	RIH
Obstetrics & Gynecology	David Nichols, MD	WIH, RIH
Orthopedic Surgery	Michael Ehrlich, MD	RIH, VAMC
Pathology (BU Intg)	Abby Maizel, MD	RWGH, TMH, MHRI, WIH, OME
Pathology (RIH)	Don Singer, MD	RIH
Pediatrics	William Oh, MD	RIH, WIH
Plastic Surgery	Armand Versaci, MD	RIH, RWGH, VAMC
Psychiatry	Ronald Wintrob, MD	BH, EPBH, RIH, TMH, VAMC(Prov Ctr)
	Patricia Recupero, MD	
Surgery	A. Gerson Greenburg, MD	RIH, TMH, VAMC
Urology	Anthony Caldamone, MD	RIH, RWGH, VAMC

gram is committed to providing a broad education in all aspects of general neurology. However, because of the depth of faculty in certain areas, special experience is offered in the treatment of cerebral vascular diseases, epilepsy, movement disorders and neuromuscular disease. The residents are encouraged to participate in research activities and to conclude investigative projects that would merit national attention.

Neurosurgery: This Brown University training program, only recently established, is based at Rhode Island Hospital and is directed by Mel Epstein, MD. This is a 6 year accredited sequence with a total of six house officers. Research endeavors as well as clinical training are conducted at Rhode Island Hospital.

Obstetrics and Gynecology:

This 4 year approved residency program is directed by David Nichols, MD. With the exception of medicine and surgery rotations at Rhode Island Hospital, the 20 residents are based at Women and Infants Hospital of Rhode Island, the sixth largest women's hospital in the United States and the only tertiary perinatal center in greater Rhode Island. There are 13 fulltime faculty providing specialty training in maternal-fetal medicine, reproductive endocrinology, and gynecologic oncology. Over 70 physicians in private practice also teach in this program. Most graduates establish their practices in New England while more than one-fifth seek additional subspecialty training.

Orthopedic Surgery: This program is directed by Michael Ehr-

lich, MD and is based principally at Rhode Island Hospital. Residents in this approved program also rotate through the Trauma Center and are required to devote a portion of their training to basic research.

Pathology: The Brown University Integrated Program in pathology, directed by Abby Maizel, MD, PhD, trains its residents at Memorial Hospital of Rhode Island, Roger Williams General Hospital, The Miriam Hospital, Women & Infants Hospital and the Medical Examiners Office of Rhode Island. Neuropathology training, under the supervision of Mary Ambler, MD, is given at Rhode Island Hospital. There are 12 residents in a 5 year training sequence. There are approved programs leading to certification in anatomic pathology, clinical pathology, forensic pathology, neuropathology, hematopathology, and dermatopathology provided by a faculty of 46 laboratory physicians and scientists. Additional training, routine or investigative, in such disciplines as blood banking, virology, microbiology and electron microscopy is also offered. A number of approved combined-training programs may also be taken, including developmental pathology and gastrointestinal pathology.

A 5 year program in anatomic and clinical pathology is offered for eight residents at the Rhode Island Hospital with additional training at Women and Infants Hospital and the Medical Examiners Office. This program is directed by Don B. Singer, MD.

William Q. Sturmer, MD, Chief Medical Examiner of Rhode Island, directs the 2 year training program in forensic pathology. Training sites include the Medical Examiner's Office of Rhode Island, the Connecticut Crime Laboratory and the Anthropology Department of the Smithsonian

Institution. Graduates of this program are presently serving in medical examiner offices in Delaware, Massachusetts and New Jersey.

Pediatrics: The Brown University residency program in pediatrics is based at the Rhode Island Hospital and, for neonatology, at Women & Infants Hospital. Pediatric residents also rotate through Emma Pendleton Bradley Hospital for child psychiatry. There are 38 resident physicians in this accredited program directed by William Oh, MD. Two of the second year residents will undertake an additional 3 years of psychiatry residency training at Butler and Bradley Hospitals and thus be qualified for certification in pediatrics, child psychiatry and adult psychiatry. This training sequence is the so-called Triple-Board Pathway, a pilot training program conducted at Brown as well as 5 other medical schools in the United States.

The training program in pediatrics is noted for its balance between academic activity and clinical experience in general pediatrics. Graduates prepare for a career either in academic pediatrics or private practice. The program is highly regarded nationally and about 40% of its graduates pursue additional subspecialty fellowship training elsewhere. In the past, most pediatrics residents originated from the northeastern states: their geographic origins are now much more cosmopolitan.

Plastic Surgery: This is the oldest accredited plastic surgery training program in New England, offering 2 years of supervised training to a total of four residents. It is directed by Lee Edstrom, MD and is based principally at Rhode Island Hospital. The program offers many research opportunities.

Psychiatry: There are 30 resident physicians in this approved

3 year program based principally at Butler Hospital but with additional training undertaken at the other Brown-affiliated hospitals. Further supervised training sites include various community mental health centers in Rhode Island and Massachusetts. Elective experiences are available within the Brown consortium of hospitals and at the Institute of Mental Health. The program emphasizes both biological and psychotherapeutic interventions as essential clinical tools in psychiatry. Opportunities for research are offered. The training program is co-directed by Patricia Recupero, MD and Ronald Wintrob, MD.

There are nine residents participating in a 2 year program in child psychiatry based at Emma P. Bradley Hospital and directed by Charles Malone, MD.

Radiology: This accredited 4 year program directed by Daniel J. Hanson, MD, currently trains 12 residents and is based at Rhode Island Hospital. Additional training is undertaken at Women & Infants Hospital and the Armed Forces Institute of Pathology, Washington, DC. Recent graduates have uniformly sought further subspecialty training and about half have entered academic medicine. The geographic distribution of the graduates is nationwide.

Surgery: The Brown University Integrated Residency in surgery is an accredited 6 year program leading to certification by the American Board of Surgery. There are 44 house officers in the program at Rhode Island Hospital, Roger Williams General Hospital, The Miriam Hospital and VA Medical Center. Off-campus rotations are arranged for subspecialties such as transplant surgery or treatment for burns. The primary goal of the program is to provide well-trained general surgeons, in an academic environment, for the

greater Rhode Island community. The program is directed by A. Gerson Greenburg, MD, PhD.

Urology: This accredited 3 year program is directed by Anthony A. Caldamone, MD. Trainees are required to complete 2 years of general surgery residency before beginning. The principal center for training is Rhode Island Hospital with both adult and pediatric urology services, and to a lesser degree, Women and Infants Hospital, Roger Williams General Hospital and the VA Medical Center.

Fellowships

Internal medicine fellowships include fully integrated programs in: cardiology, clinical pharmacology, critical care medicine, endocrinology and metabolism, gastroenterology, geriatric medicine, hematology/oncology, infectious diseases, pulmonary diseases, nephrology and rheumatology.

Pediatric fellowships include: endocrinology and metabolism, hematology/oncology, child development and developmental disabilities, and ambulatory pediatrics. The neonatology/perinatology fellowships are 3 year programs based at Women & Infants Hospital. Of the 37 graduates of this highly regarded fellowship program, 34 hold professorships at US medical schools and 4 are directors of neonatology at major academic centers.

Radiology fellowships are offered in cross-sectional imaging, interventional and vascular radiology, and radiologic research.

Maternal-fetal medicine fellowships, lasting 2 years, require prior completion of residency training in obstetrics and gynecology. All the graduates of this program, thus far, have entered academic medicine.

Post-doctoral Training Pro-

Table 2. Brown University Affiliated Fellowship Programs

Fellowship	Program Director	Principal Training Sites
Alcoholism & Drug Abuse	David Lewis, MD	RWGH, BH
Ambulatory Pediatrics	John O'Shea, MD	RIH
Cardiology	David Williams, MD	RIH
Cardiology	Candace McNulty, MD	TMH, MHRI, RWGH, VAMC
Child Dev & Dev Disabil	Siegfried Pueschel, MD	RIH
Clinical Pharmacology	Darrell Abernethy, MD	RWGH
Combined Imaging	Daniel Hanson, MD	RIH
Critical Care Medicine	William Kaye, MD	TMH
Developmental Pathology	Don Singer, MD	RIH, WIH, OME
Endocrinology & Metabolism	Ivor Jackson, MD	RIH
Gastroenterology	Joseph Tucci, MD	RWGH, VAMC
Geriatric Medicine	Walter Thayer, MD	RIH, RWGH
Hematology/Oncology (Brown Affiliated Program)	Marsha Fretwell, MD	RWGH
Infectious Diseases	Louis Leone, MD	RWGH, VAMC, TMH, MHRI, RIH
	Stephen Zinner, MD (adult)	TMH, MHRI, RIH
	Georges Peter, MD (pediatric)	RWGH, VAMC
Maternal-Fetal Medicine	Donald Coustan, MD,	WIH
Neonatology	William Oh, MD	RIH, WIH
Nephrology	Joseph Chazan, MD	RIH
	J. Gary Abuelo, MD	
Neuropathology	Mary Ambler, MD	TMH, RIH
Ped Hematology/Oncology	Ed Forman, MD	RIH
Ped Metabolism & Nutrition	Philip Gruppuso, MD	RIH
Pulmonary Diseases	Sidney Braman, MD	RIH, VAMC, MHRI, RWGH
Rheumatology	Edward Lally, MD	RWGH, RIH, VAMC
Vasc & Interventional Radiology	Daniel Hanson, MD	RIH

gram in Research on Substance Abuse, Treatment and Intervention: This is a training program conducted within the administrative structure of the Center for Alcohol and Addiction Studies at Brown University. It provides research training for behavioral and social scientists and health care professionals who wish to pursue a career in alcohol and/or drug abuse research.

Address correspondence to: Fred J. Schiffman, MD, Department of Medicine, The Miriam Hospital, 164 Summit Avenue, Providence, RI 02906

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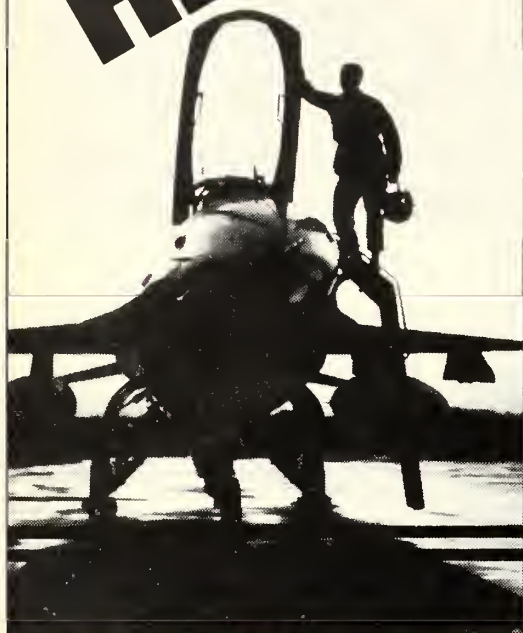
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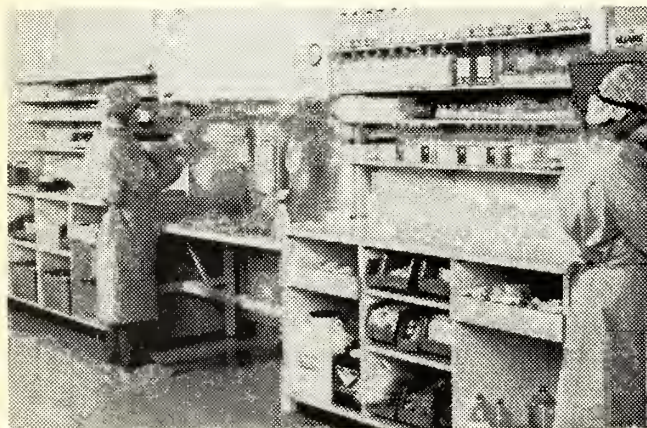
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Resident Physicians' Research Day

The Fourth Annual Meeting of the Rhode Island Chapter of the American College of Physicians and the Brown University Department of Medicine

Fred J. Schiffman, MD

On March 28, 1990, the Brown University Department of Medicine and the Rhode Island Chapter of the American College of Physicians held their Fourth Annual joint meeting which included scientific presentations by Brown University resident physicians in medicine. House officers from each of the Brown University teaching hospitals had previously submitted abstracts of clinical investigations or clinical vignettes which they had worked on during the last year. Additionally, fellows in Internal Medicine sub-specialty programs, were encouraged to submit abstracts of work for presentation as posters. A panel had evaluated and ranked submissions and on March 28, the top ones were presented orally or in poster form.

Four years ago, Dr H. Denman Scott who was ACP Governor for Rhode Island and Dr Paul Calabresi, Chairman of Brown's Department of Medicine, began a cooperative effort which incorporated presentation of residents' research into a day-long meeting whose agenda included a panel

discussion of a timely topic impacting upon health care, distinguished speakers from the American College of Physicians and the presentation of the Irving Beck Laureate Award to an outstanding internist and member of the American College of Physicians, Rhode Island Chapter for long and sustained career service to their patients.

Over the last several years, this meeting has been held in March or April and it has become a highlight for the Brown affiliated hospitals with Internal Medicine training programs. Program Directors at The Miriam Hospital, The Memorial Hospital of Rhode Island, Rhode Island Hospital, Roger Williams General Hospital and the VA Hospital begin organizing activities almost 9 months in advance of the actual meeting. They, with their chief residents, house officers and attending physicians identify research projects or clinical vignettes which may be appropriate for presentation at the Annual Meeting. Working with faculty mentors, residents write up in abstract form, material to be considered for presentation at the Annual Meeting. The majority of submissions are abstracts of clinical vignettes (interesting or unusual patient stories with important teaching points). However, basic research, clinical trials or reviews of the literature can be

included if the work was done during a resident's training tenure at one of the Brown hospitals. Abstracts are reviewed by the five program directors, given a numerical rank and the top 15 or 16 are chosen for oral presentation at the meeting. Those which are not selected for such presentation are considered for presentation as a poster. Fellows in Internal Medicine sub-specialty programs are invited to submit abstracts but only for poster competition since it is felt that their work may be more readily presented at national forums other than the American College of Physicians competition. Residents are also encouraged to submit their work to the National ACP Meeting where, on a grander scale, oral presentations and poster sessions are held. Several Brown residents have been selected to present work at this session.

The submitted abstracts this year were evaluated and rated by the training program directors and then using a computer program developed by Dr Bryson Ley, scores were generated which took into account many subtleties of the ranking process. This year, 16 abstracts were selected for oral presentation with representation from each of the hospitals. Twenty-five abstracts were chosen for poster presentation. Res-

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Resident Physician Prize Winner

idents making oral presentations were given 7 minutes to describe their work with 2 minutes allowed for questions and answers from the assembled group. Between a morning and afternoon session, the participants at the 1990 Scientific Meeting were asked to view the posters and discuss the work with presentors.

The program this year also featured a panel discussion of the Canadian Health Care System. The panel included several prominent ACP members from Canada who addressed the topic of "What Can the United States Learn from Canada?" Debbie Prout, director of policy for the American College of Physicians and Edward P. Maynard, MD, FACP, President of the American College of Physicians, spoke at the luncheon held in the Grand Ballroom at the Omni Biltmore Hotel and updated participants on current ACP activities.

Following presentation of scientific work, the Irving A. Beck Laureate Award was given to Michael DiMaio, MD and competing residents received awards as judged by the visiting panel from Canada and other dignitaries present. Cash awards and a plaque were contributed by Marion-Merrill Dow Pharmaceuticals. Three awards were given for clinical vignettes, 2 for clinical investigations and 2 for the best posters. While in some ways the presentors compete with each other for prizes, it has been the goal of the organizing committee to deemphasize award-seeking behavior and foster meaningful participation and high quality, scholarly work by as many participants as possible.

All of the abstracts of oral presentations have been reproduced here and abstracts of the award winning posters have as well.

It is felt that research by medical residents is an important part



(L) Paul Calabresi, MD, Chairman, Brown Department of Medicine;
(R) Abraham Kocheril, MD, First Prize Poster Competition.



(L) Paul Calabresi, MD, Chairman, Brown Department of Medicine;
(R) Anne Ruggieri, MD, first prize Clinical Vignette Competition.

Residents' Research Day

March 28, 1990



(L) Paul Calabresi, MD, Chairman, Brown Department of Medicine;
(R) Jane Carter, MD, second prize poster competition.



(L) Peter Cohn, MD, tied first prize, clinical investigation; (C) Paul Calabresi, MD, Chairman, Brown Department of Medicine; (R) C. Pyne, MD, tied first prize, clinical investigation.

of the Brown University Internal Medicine training program for several reasons:

1. A more critical manner of thinking is fostered.
2. Sharper focus is brought to bear on clinical problems and disease processes at a particularly formative period of time.
3. Mentoring relationships are fostered.
4. Non-specialty "hobbies" are developed.
5. The resident gains a sense of academic accomplishment and a foundation is constructed for further scholarly pursuit.
6. The resident learns to read and write "the literature."
7. Teaching others is fostered.
8. Active resident research enhances the intellectual ferment in the institution and potentially expands the range of career options and interests.

It is hoped that the Residents Research Day will continue to evolve over the years and that even more residents will participate. Besides the intellectual merit discussed above, this meeting has fostered closer ties between the American College of Physicians, Brown's Internal Medicine Department, the program directors and all of our medical residents.

Scientific Papers Presented by Resident Physicians from the Hospitals of Rhode Island at the 1990 Annual Scientific Meeting of the Rhode Island Chapter of the American College of Physicians

In each of the scientific abstracts, the resident-physician is identified by hospital of origin and medical school; the faculty sponsor is identified by faculty rank. All faculty positions are at Brown University.

Abstracts designated by asterisks were awarded prizes by the judges.

***1. Echocardiatic Assessment of Atrioventricular Valvular Regurgitation in Pregnancy**

A. Kocheril, MD, Miriam Hospital (New York Univ)

A. Sadaniantz, MD, Assistant Professor of Medicine

Systolic murmurs are common findings during pregnancy, the etiology of which may be A-V valvular regurgitation or flow murmurs due to increased cardiac output. A previous study has shown an increased frequency of tricuspid regurgitation (TR) during pregnancy, although that study was done on women in various stages of pregnancy.

The purpose of our study is to assess longitudinal changes in A-V valvular regurgitation with pregnancy. We studied 11 pregnant women by M-mode, 2-D, pulsed and color Doppler (D) echocardiography at 8 months of pregnancy and then again in the same subjects 1 month after delivery, and compared them with 7 nonpregnant age-matched controls. Exclusion criteria were: 1) exercise more than 3 times per week for greater than 20 minutes each time, 2) significant medical illness, and 3) any morphologic valvular abnormality by M-mode or 2-D echocardiography at any stage. Jet areas and atrial dimensions were measured in the 4-chamber view by digitizing. Mild mitral regurgitation (MR) or TR was defined by color Doppler jet area less than 25% of the corresponding atrial size, moderate being 25-50% of atrial size, and severe greater than 50% of atrial size. Our results are as follows:

	8 months pregnant	1 month after delivery	Control
MR by (D)*	2/11 (18%)	5/11 (45%)	4/7 (57%)
TR by (D)*	6/11 (54%)	6/11 (54%)	6/7 (86%)
SEM	5/11 (45%)	0/11 (0%)	1/7 (14%)
Holosystolic murmur	0/11 (0%)	0/11 (0%)	0/7 (0%)

*All subjects had mild or less regurgitation; none were moderate or severe. We found no statistically significant differences by chi-square analysis in any of the above parameters among the groups. We found no significant differences in frequency or severity of MR or TR in the same subjects at 8 months of pregnancy compared to 1 month after delivery, or compared to the controls. Flow murmurs are common findings in women 8 months pregnant, without associated significant regurgitant jets by Doppler echocardiography, but disappear at 1 month after delivery.

***2. Cardiac Catheterization Prior to Electrophysiologic Studies**

P. Cohn, MD, Rhode Island Hospital (Rob WoodJohnson Sch Medicine)
C. Chmielewski, MD, Clin Assistant Professor of Medicine

The long term prognosis after symptomatic ventricular tachycardia or cardiac arrest, in the absence of acute myocardial infarction, has been significantly improved by electrophysiologic testing and the implantable defibrillator. Studies have recommended cardiac catheterization prior to electrophysiologic testing, as there is a high incidence of significant coronary artery disease in this patient population. We studied patients who presented in symptomatic ventricular tachycardia or sudden cardiac death from 1984 to June of 1989. A retrospective analysis of cardiac catheterizations in these patients was performed. A total of 130 patients presented with ventricular tachycardia and had EPS studies. Of 69 patients undergoing cardiac catheterization, 53 had significant coronary artery disease (70% or greater luminal stenosis). 17 patients had 3 vessel disease, 19 had 2 vessel disease and 17 had single vessel disease. A total of 75 patients who had survived a cardiac arrest underwent EPS studies. Of the 52 patients who were catheterized, 39 had significant disease. 21 patients had 3 vessel disease, 12 patients had 2 vessel disease and 6 patients had single vessel disease. The study confirms that patients who present with ventricular tachycardia and sudden death in the absence of a myocardial infarction, do have a high incidence of significant coronary artery disease. In both groups the percentage of severe disease, classified as 2 to 3 vessel involvement, is quite high. This was especially evident in the sudden death group. We conclude that catheterization is necessary prior to EPS in the patients presenting with the above diagnoses.

***3. Post-Partum Renal Vein Thrombosis in a Patient with Pre-eclampsia**

A. Ruggieri, MD, Miriam Hospital (Brown-Dartmouth)
R. Mahnensmith, MD, Assistant Professor of Medicine

A 20-year-old previously normotensive prima gravida with a history of ITP presented with accelerating hypertension and abdominal pain in her 31st week of pregnancy. She was hospitalized. BUN and serum creatinine were normal. Proteinuria was present as a new finding. She was treated with hydralazine and underwent C-section at 32 weeks. Abdominal pain resolved after delivery but BP remained elevated. She was discharged on hydralazine and methyldopa. Left lower quadrant pain reappeared with fever to 103° one week later. A D&C was performed for presumed detained placenta. No placenta was found. A working diagnosis of pelvic thrombophlebitis was made and heparin was initiated. Her BP remained severely elevated despite therapy. Abdominal pain and fever persisted. An abdominal CAT scan showed a markedly enlarged left kidney without hydronephrotic changes. Also present was an enhancing peripheral rim nephrogram consistent with renal edema and renovascular compromise. The renal vein was enlarged but the renal artery was not visible. An inferior venacavagram demonstrated left renal vein thrombosis confirmed by digital arteriogram. Based on her acute hypertensive presentation, persisting severe hypertension, fever, pain, and radiographic findings, it was concluded that she had suffered acute renal vein thrombosis (RVT) with renal infarction. A left nephrectomy was performed at this point, revealing renal infarction and complete occlusion of the renal vein by clot at least 4 weeks old. Fevers dissipated and BP normalized. She has subsequently required eye surgery for hypertensive induced retinal edema and detachment.

RVT is most often a complication of chronic nephrotic syndrome and is usually indolent. It usually does not cause renal infarction. Rare case reports of acute RVT complicating pregnancy exist. Pressure on the left ovarian vein by a gravida uterus may be an initiating process, because the left ovarian vein drains directly into the left renal vein. A mild hypercoagulable state which accompanies pregnancy may also contribute. This case presents a rare complication of pregnancy and illustrates an unusual mechanism for late trimester pregnancy-associated hypertension.

***4. Palmar Fasciitis-Arthritis is a Harbinger of Occult Malignancy**

E. Carter, MD, Memorial Hospital (Geo Washington Univ)
F. Fawaz-Estrup, MD, Clin Assistant Professor of Medicine
D. Ettensohn, MD, Assistant Professor of Medicine

Palmar fasciitis-arthritis is a paraneoplastic syndrome thought to be a variant of reflex sympathetic dystrophy. While primarily associated with ovarian carcinomas, it has been reported in patients with breast, pancreatic, colon, and lung tumors. This rheumatologic symptom complex is frequently the first manifestation of malignancy. A 63-year-old female presented with a 3 month history of rapid onset polyarthritis unresponsive to NSAIDs. There was no history of fever, chills, night sweats, dysphagia, hemoptysis, skin rash, abdominal distention, or change in bowel habits. A complaint of mild dyspnea was felt to be smoking-related. Rheumatologic evaluation (ESR, ANA, RF, anti-SSA, anti-SSB, Sclero 70) was negative. Over the next 2 months she developed progressive contractures of both hands and atrophy of the overlying skin. Skin biopsy showed slight thickening of the dermal collagen bundles but no evidence of scleroderma. Steroids did not slow progression of deformity or give symptomatic relief. She developed worsening dyspnea. Chest X-ray revealed a diffuse right-sided interstitial pattern. PFTs revealed moderate obstruction and bron-

chodilators partially relieved her symptoms. A lower GI bleed led to hospitalization; a barium enema showed a polyp in the ascending colon and mammography revealed a questionable lesion in the right breast. The patient refused evaluation until hemoptysis ensued. Cytologic evaluation of bronchoalveolar lavage cells revealed adenocarcinoma. She refused further therapy and died two weeks later. Autopsy revealed a giant cell lung carcinoma metastatic to spleen, liver, and lymph nodes. Palmar fasciitis-arthritis is a paraneoplastic syndrome, the presence of which indicates metastatic occult malignancy and should prompt aggressive evaluation to identify the primary site.

***5. Simultaneous Babesiosis and Lyme Disease**

G. Bubly, MD, Miriam Hospital (Univ Massachusetts)
J. Boyce, MD, Assistant Professor of Medicine

In July 1989, a healthy 65-year-old white male Block Island resident sought medical attention for an annular, erythematous rash with central clearing on his left leg. Dicloxacillin was prescribed for presumed cellulitis and the rash gradually faded. Low grade fevers, myalgias, and a borderline-positive Lyme titer prompted his physician to switch his therapy to doxycycline. One week later, he developed intermittent fevers to 40°C, rigors and drenching sweats. Therapy was changed from doxycycline to ampicillin/clavulanate and he was referred to this hospital. On further questioning, he described "hundreds" of previous tick bites, but denied transfusion, splenectomy, or travel to areas endemic for babesiosis or malaria. Examination revealed a temperature of 38.3°C and rigors, a faintly visible well-circumscribed oval rash on his left leg, and scleral icterus. A peripheral blood smear showed intraerythrocytic and extra-cellular parasites, including one tetrad form diagnostic of babesiosis. Clindamycin, quinine and doxycycline were begun for presumed simultaneous babesiosis and Lyme disease. Antibody titers to *Babesia microti* (1:1024) and *Borrelia burgdorferi* (1:2048) confirmed both diagnoses. The patient defervesced after three days of treatment and recovered completely.

This is only the third well-documented case of simultaneous symptomatic infection with *B. microti* and *B. burgdorferi* reported in the literature. Furthermore, this represents only the second reported case of babesiosis acquired in Rhode Island. Physicians in endemic areas should be aware of the possibility of dual infection.

***6. Intravascular Coagulation, Fibrinolysis, and Acute Lung Injury in Post-Traumatic Patients**

C. Pyne, MD, VA Medical Center, Providence (Hahnemann)
A. Carvalho, MD, Associate Professor of Medicine

In a prospective study of 23 patients with uncomplicated long bone fractures, we assessed intravascular coagulation (IVC), fibrinolysis (F), and development of acute lung injury. To monitor endothelial cell injury, we measured plasma von Willebrand factor (vWF) levels. In addition to routine screening tests for IVC, we measured plasma D-dimer levels. To assess whether the fibrinolytic response was appropriate for the degree of blood activation we monitored plasminogen, plasminogen activator inhibitors (PAI), and fibrin(ogen) degradation products (FDP). Samples were obtained on admission and on days 2 and 4. Complete blood counts, platelet count, and arterial blood gases were done daily. Chest radiographs were obtained on admission and repeated in patients with hypoxia ($pO_2 < 60$, Group 1). Eleven of 23 patients developed $pO_2 < 60$ (Group 2) on the 2nd, 3rd, or 4th days, although none had $F_iO_2 > 0.5$, indicating mild lung injury. The vWF levels in Group 1 ($n = 12$) were 277 ± 50 (mean \pm SEM) at baseline and remained unchanged for the 4 days of observation; whereas in Group 2 ($n = 11$) vWF levels were higher (322 ± 55) and continued to rise (393 ± 54). Both groups had vWF levels significantly higher than normal ($n = 41$, 97 ± 3). IVC was present in both groups of patients, as evidenced by increased D-dimer levels, but more so in Group 2 than Group 1. Plasminogen and FDP levels remained normal in both groups. PAI levels were significantly higher in both patient groups than normal ($p < 0.01$). Our data show that IVC with impaired fibrinolysis occurs in post-trauma patients and may contribute to their lung injury and frequent thromboembolic complications.

***7. Acute Renal Failure Resulting from Spontaneous Athero-embolism Due to Anti-Coagulant Therapy**

L. Stone, MD, Miriam Hospital (St Louis Univ)
R. Mahnensmith, MD, assistant Professor of Medicine

A 65-year-old man with a history of hypertension, a transient ischemic attack, and stable mild renal insufficiency was hospitalized because of left arm and leg weakness and blurred vision. BP was 200/100. BP was lowered with clonidine. Full anticoagulation with intravenous heparin was begun. From the first hospital day, the patient's creatinine showed a progressive elevation, from 3.3 mg% on admission to 6.1 mg% on the 8th hospital day. This was initially attributed to IV radiocontrast and blood pressure lowering. His creatinine declined to 4.1 mg% by the 20th hospital day, but then suddenly showed a steady inexorable daily climb to 10.8 mg% by the 35th day. This deterioration was characterized by high output of dilute urine and moderately severe hypertension. Renal echo was normal. Urinalysis showed only trace protein, rare WBCs, and rare granular casts. The great toe of his left foot became purple and painful. Heparin,

which had been administered for 33 of 35 days, was discontinued and renal biopsy was performed. The biopsy revealed multiple arteries and arterioles of various sizes containing cholesterol emboli. Some glomeruli were sclerosed, others were hypercellular. The interstitium showed mild inflammation with tubular fibrosis and atrophy.

This patient had not undergone any invasive angiographic procedures. His course is consistent with the rare occurrence of spontaneous renal and distal atheroembolism induced by anticoagulation. Renal function did not improve; 7 of 10 toes developed microinfarctions, and peripheral eosinophilia later evolved. He has required maintenance dialysis.

8. A Guatemalan Woman with Abdominal Pain and Peripheral Eosinophilia

S. Blood, MD, Rhode Island Hospital (Univ Vermont)

J. Kizirian, MD, Clin Assistant Professor of Medicine

The patient, a 40-year-old Guatemalan woman who recently emigrated to the United States, presented with a 3 week history of abdominal pain and passage of large, round worms per rectum. She also complained of headache, anorexia and nausea. Her past medical history was significant for pica, manifested as consumption of clay tile, which she developed during her first and only pregnancy.

Physical exam revealed a thin, Hispanic woman with moderate abdominal discomfort. Pertinent physical findings included pale conjunctivae and a diffusely tender abdomen with hyperactive bowel sounds. Stool was occult blood negative. Lab findings included iron deficiency anemia, leukocytosis, and an absolute eosinophilia of 8832. Stool specimens contained ova and the adult form of *ascaris lumbricoides*. Barium swallow outlined the worms in the GI tract. Because intestinal ascariasis does not usually produce eosinophilia, a work-up for other parasitic infections was done. A toxocara titer was markedly positive at 1:2048, suggesting exposure to toxocara in this patient who manifested no end-organ involvement by toxocara or visceral larvae migrans.

The patient was treated with a 3 day course of mebendazole. Follow up stool specimens were parasite free. The patient's iron deficiency anemia was presumed to date back to her pregnancy. As is occasionally seen in the iron deficiency state, the patient developed geophagia which is thought to satisfy a craving for a lack of dietary iron. Unfortunately, geophagia may have predisposed her to soil-borne parasitic infections such as ascariasis and toxocariasis which are indigenous to Central America. Iron replacement was initiated in hospital to treat the anemia and curb the tendency toward geophagia to prevent recurrence of parasitic infection. This case is an example of ascariasis, a common infection in the Third World, but uncommon in the Northeastern United States, in a patient predisposed to parasitic infections due to her unusual habit of geophagia.

9. Mollaret's Meningitis

M. McCartney, MD, Roger Williams General Hospital (Wayne State Univ)

P. O'Dowd, MD, Clin Assistant Professor of Medicine

A 37-year-old white female with a history of recurrent aseptic meningitis in 1972 and 1975 and chronic earaches and sinusitis was admitted with complaints of severe headaches, N/V, photophobia, nuchal rigidity and myalgias. She denied fever, chills, respiratory, GI or GU symptoms. The patient had taken antihistamines and doxycycline for sinusitis and had no allergies. Pertinent physical exam showed nuchal rigidity and an otherwise nonfocal neurological exam. Sinus films and chest X-ray were negative and LP revealed normal OP, elevated WBC (220) with 90% lymphs, elevated protein (206) and normal glucose. Gram stain was negative, as were AFB, cryptococcal antigen and fungal studies. A parameningeal focus was ruled out with MRI and it was felt that her history was consistent with Mollaret's meningitis, a rarely reported entity of recurrent idiopathic aseptic meningitis.

Transient neurologic disturbances including coma, sz, syncope, diplopia, dysarthria, dysequilibrium and facial paralysis have been reported. The patients are usually febrile. Onset may occur at any age with episodes recurring over 3-5 years. The CSF shows pleocytosis with mononuclear cell predominance. Large endothelial ("Mollaret") cells may be seen but are not necessary for the diagnosis. Protein is usually elevated with normal glucose. It is speculated by Barakat that this dz may share a common origin with Familial Mediterranean Fever and as such a provocative test with metamrinol infusion may aid in the diagnosis. Treatment is supportive although it is speculated that colchicine may prevent recurrence.

This unusual case illustrates that structural abnormalities need not be present in cases of recurrent aseptic meningitis.

10. Lactobacillary SBE in a Patient with a Porcine Mitral Valve after a Dental Procedure Despite Prophylactic AntiBX

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R. Riley, MD, Clin Associate Professor of Medicine

A 68-year-old woman with a history of severe mitral regurgitation 2 years status post a porcine valve replacement had

dental work followed by appropriate IM injection of AMP/PCN/GENT. Two weeks later she presented to the hospital with 5 days' history of night sweats, chills and fevers to 103. On physical exam she had a temperature of 102pr, pulse 100 and regular, and BP of 140/80; her lungs were clear and cardiac exam regular, without a murmur. There was no evidence of embolic events for petechiae on right thumb and fifth finger, and neurologic exam was normal. Labs: Hgb was 12.3 with a normal smear, WBC was 6.4 without a left shift and platelets, 273 k. Electrolytes were within normal limits. Four out of four blood cultures were positive for *Lactobacillus*. Echocardiogram revealed a small vegetation on the mitral valve without evidence for regurgitation. Within 72 hours on PCN 12 mill. U/day and Gentamicin, she defervesced and the bacteremia cleared. She was sent home to complete a 6 week course of IV therapy, however re-presented in 10 days with recurrent fevers and chills and negative blood cxs. These cxs. cleared with increasing the PCN to 24 mill. U/day. Sero-cidal levels obtained previously showed adequate inhibitory titres, but poor cidal titres. It was decided to continue with the increased antibx regimen. She presented 2 weeks later with progressive malaise, fatigue, and dyspnea on exertion and was found to have low-grade temperature and a new systolic murmur consistent with mitral regurgitation. Repeat echocardiogram confirmed this as well as demonstrating marked growth of the vegetation. She underwent a mitral valve replacement and remains on long-term IV antibiotics post-operatively. *Lactobacillus* is a rare cause of sub-acute SBE with only moderate response to high dose antibx regimens. This case demonstrates an unfortunate failure of antibx prophylaxis during dental work.

11. A Case of Ciguatera Poisoning

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P. O'Dowd, MD, Clin Assistant Professor of Medicine

A 54-year-old Spanish man presented with severe GI distress after sharing a fish soup with his family. Their symptoms began within 1 hour of their meal which was homemade that morning with uncanned vegetables, potatoes and a large fish head purchased from a streetside vendor in Federal Hill. The wife and daughter, who had smaller portions, promptly improved but the father's condition deteriorated rapidly to a paralytic coma requiring intubation. On examination he was diaphoretic, hypothermic, hypertensive and tachycardic with markedly miotic pupils, upbeat nystagmus and areflexia. Toxic ingestion was suspected, including ciguatera toxin and organophosphates.

The patient was unresponsive to naran, mannitol and pralidoxime, but with supportive therapy gradually resumed consciousness and completely recovered within 72 hours. His course was complicated only by alcohol withdrawal and aspiration pneumonia. Samples of the soup were tested for ciguatera toxin.

Ciguatera fish poisoning is not uncommon in tropical reefs with concentration of the toxin up the food chain, however should be considered in unlikely locations due to importation of fish products. Interestingly, ciguatera toxin is not included in neurology texts as a neurotoxin capable of inducing coma, but this case demonstrates that it should be added to the differential diagnosis of a comatose patient with recent fish ingestion.

12. Auscultated Forced Expiratory Time as a Clinical and Epidemiologic Test of Airway Obstruction

S. Patel, MD, Memorial Hospital (Grant)
D. Kern, MD, Assistant Professor of Medicine

Objective: To determine the validity of current dogma that forced expiratory time (FET) is an excellent clinical test of airway obstruction yet epidemiologically useless due to excessive intrasubject variability.

Subjects and Methods: 229 white male plumbers and pipefitters were evaluated by spirometry, chest radiography and a standardized respiratory questionnaire during a union-sponsored asbestos screening program. Subjects were classified as having large airway obstruction (LAO), small airway obstruction (SAO), or no obstruction, on the basis of standard spirometric prediction equations. Two physicians, blinded to clinical and spirometric data, independently measured FET while auscultating the trachea with a stethoscope. FET was defined as the time taken for an individual to forcefully exhale from total lung capacity until airflow became inaudible. Five such times were recorded for each subject. The mean of the 3 values having the narrowest range was deemed the FET for calculating test sensitivity and specificity. Based on previous literature, an FET ≥ 6 seconds was considered abnormally prolonged.

Results: 204 subjects completed both spirometry and FET testing. 66 had LAO, 6 SAO, and 132 no obstruction. 83% had 3 FETs reproducible within a range of ≤ 1 second. In detecting LAO, the sensitivity of FET was 92% and the specificity 41%. In detecting SAO alone, the sensitivity of FET was 67% and the specificity 42%. Overall, then, FET misclassified 58% of non-obstructed subjects.

Conclusion: Although a simple, sensitive, and fairly reproducible clinical test of large airway obstruction, FET can be recommended as neither a clinical nor epidemiologic tool because of extremely poor specificity.

13. Prevalence of Crackles in Blue Collar Workers

T-J. Cheng, MD, Memorial Hospital (Taipei, Harvard)
D. Kern, MD, Assistant Professor of Medicine

Objective: To determine the prevalence of bibasilar lung crackles in a working male blue collar population having

minimal exposure to fibrogenic dust, their specificity for bilateral pleuropulmonary disease processes, and the inter-observer variability of such crackles.

Subjects: All 200 male carpenters, age ≤ 65 , who completed an examination offered to the 1009 working members of the RI District Council.

Methods: Using standardized definitions and protocols, 2 physicians, blinded to clinical data, independently auscultated the subjects' posterolateral lung bases during inhalation from functional residual capacity (FRC) to total lung capacity (TLC). Subjects completed standardized respiratory questionnaires, performed pulmonary function tests, and had chest roentgenography.

Results: The prevalence of bibasilar crackles ranged from 0.03-0.06. When the definition required that crackles be auscultated by both physicians, the prevalence was 0.009 in the 108 subjects randomly selected to be examined by both observers. The specificity of bibasilar crackles auscultated by both physicians was 99%. The kappa statistic of interobserver variability was 0.09.

Conclusion: In spite of excessive interobserver variability, the results suggest that male blue collar workers having minimal fibrogenic dust exposure will only rarely be found to have bibasilar crackles by both of 2 examining physicians. Furthermore, the specificity of crackles, so defined, will usually be acceptable for study of both individuals and populations at risk of bilateral pleuropulmonary disease.

14. A Herald Bleed

G. Does, MD, Memorial Hospital (Brown University)

M. Miller, MD, Associate Professor of Medicine

A 78-year-old male was brought to the hospital after being found in a "pool of blood." The patient was alert, talkative, hypothermic and orthostatic. Nasogastric drainage and stools were positive for occult blood. The patient had recently been taking aspirin "by the handful." Past medical history was significant for a small bowel obstruction with lysis of adhesions 1 year prior to admission. Endoscopy revealed the stomach to be full of blood, without an obvious source of bleeding. Treatment consisted of blood products, intravenous fluid, H_2 blockers and vitamin K. The hemoglobin eventually stabilized. Hematemesis accompanied by hypotension developed on the 6th hospital day. An exploratory laparotomy was performed to identify the site of bleeding and a partial gastrectomy was performed. On the 3rd post-operative day massive hematemesis recurred. "Oozing of blood" was noted during endoscopy at the site of the anastomosis. The patient was emergently taken to the operating room and was found to have a bleeding aorto-esophageal fistula. Despite aggressive fluid and medical resuscitation, the patient died.

This case represents one of the more unusual causes of upper GI bleeding. The classic triad of pain, sentinel hemorrhage and final exsanguination described by Chiari in 1914 was not entirely met in our patient since pain was notably absent. Could it be that the consumption of aspirin "by the handful" alleviated the pain and promoted bleeding by direct and by indirect mechanisms thereby adding "fuel to the fire"?

15. Aortic Coarctation: A Surprise Diagnosis in a 41-Year-Old Woman with Angina and Refractory Hypertension

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R. Mahnensmith, MD, Assistant Professor of Medicine

A 41-year-old female with a history of refractory hypertension was admitted to the hospital for recurrent chest pain with ECG changes. High blood pressure had been present for at least 8 years and was difficult to normalize in spite of multiple drug therapy. Chest pressure, intermittently present for 2 months, followed a crescendo course over the 3 days prior to admission. An episode unrelieved by sublingual nitroglycerin prompted admission. Physical exam revealed right and left arm blood pressure of 160/90, grade II retinopathy, a soft systolic chest murmur, diminished femoral pulses, and poor pedal capillary refill. Blood pressure was 80 systolic in her leg. EKG showed lateral T-wave inversion. Rib notching was evident on chest radiograph. Chest pain recurred despite IV nitroglycerin. Cardiac catheterization demonstrated aortic coarctation just distal to the left subclavian artery and normal coronary arteries. Plasma renin activity measured supine immediately before and 60 minutes after 25 mg captopril per os dramatically increased from 2.8 to 19.1 ng/ml/hr.

This case illustrates classic historical, physical, and radiographic features of aortic coarctation. In addition, it demonstrates that the renin response to captopril, recognized as a sensitive and specific test for renal artery stenosis, may be useful in detecting aortic coarctation.

16. Meningioma Masquerading as Cervical Syndrome

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B. Ley, MD, Assistant Professor of Medicine

Cervical syndrome is a common condition in ambulatory medicine. A 59-year-old woman carried this diagnosis for

2 years before developing incompatible neurological deficits.

The patients initial complaint was a dull, constant, occipital headache, radiating bifrontally, and exacerbated by neck flexion. Cervical spine films showed degenerative changes. Eighteen months later she developed urinary frequency and paresthesias of the hands and feet, and 6 months thereafter diplopia and ataxia. Neurological examination at that time revealed flat affect, bilateral horizontal gaze nystagmus, a wide based ataxic gait, and a positive Romberg. Plantar reflexes and sensory findings were variable. Lumbar puncture revealed an opening pressure of 7 mm Hg, 4 lymphocytes and protein of 164 mg/dl. Computerized tomography (CT) of the brain was normal whereas magnetic resonance imaging (MRI) revealed a 2.8 cm extracranial mass at the foramen magnum with posterior displacement of the medulla. A meningioma was found at surgery.

Meningiomas account for 13-18% of symptomatic and 33% of asymptomatic brain tumors. However, meningiomas in the region of the clivus and foramen magnum are uncommon. Published cases similar to the one presented describe a syndrome of headache exacerbated by neck motion, fluctuating neurological deficits, and nystagmus. In the evaluation of cervical syndrome with fluctuating neurological deficits or nystagmus, tumors of the posterior fossa and high spinal cord should be considered. Furthermore, MRI is superior to CT in detecting these lesions.

17. Problem Solving in Alcoholic Pancreatitis: Role of Endoscopic Retrograde Cholangiopancreatography (ERCP)

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E. Feller, MD, Clin Assoc Professor of Medicine

We reviewed records of 96 patients with alcohol abuse and pancreatic disease who had ERCP to assess its utility in patient management. Indications for ERCP included pre-operative assessment of recurrent or intractable pain in chronic alcoholic pancreatitis (43), etiology of unexplained acute pancreatitis (15), diagnosis of cholestasis (11), differentiation of pancreatic carcinoma from chronic pancreatitis (13), evaluation of cholangitis or sepsis (6), preoperative assessment of a pseudocyst (5), delineation of site of duct disruption in pancreatic ascites or pancreatico-pleural fistula (3).

In the 51 patients having ERCP to guide surgical strategy, unexpected, relevant findings were also seen in 7 patients. These included common bile duct stones (2), ampullary stenosis or biliary stricture (2), pancreatic carcinoma (1), pseudocyst (2), and gastric ulcer (1). In acute pancreatitis, 5 of 15 patients had potentially remediable disease, including common bile duct stones (2), gallstones (1), pancreatic carcinoma (1), and ampullary stenosis (1). ERCP was also sensitive in evaluating alcoholic patients with unexplained cholestasis, biliary sepsis, or possible pancreatic carcinoma. By defining duct anatomy, ERCP may determine surgical approach for pain relief, assess complications, and exclude other treatable pancreatic or biliary disorders.

18. Pure RBC Aplasia, AIDS and B19 Parvoviral Infection

D. Marcoux, MD, (Med Coll Wisconsin)

M. Safford MD, Clin Instructor of Medicine

F. Schiffman, MD Assoc Professor of Medicine

A 26-year-old white homosexual male presented with complaints of progressive shortness of breath, headache, and the sensation of his "brain was starved for oxygen" over 4-6 weeks. He denied cough, fevers, weight loss, hematemesis, melena, hematochezia and hematuria. He was taking no medications and denied illicit drug and all alcohol use. On physical exam he appeared very pale. Oral temperature was 38°C. Blood pressure was 130/70 and heart rate 120 without orthostasis. There was no icterus, lymphadenopathy or splenomegaly. Lung and heart exams were normal except for tachycardia and a soft flow murmur. Stool was negative for occult blood. Hb: 4.2 mg/dl, WBC: 8,200 mm³: 59 segs, 2 bands and 27 lymphs. Platelets: 519,000 mm³. Peripheral smear: platelets and WBC normal in number and appearance. RBC were of uniform size and shape with no macro or microcytosis and no evidence of hemolysis rouleaux or polychromatophilia. Reticulocytes: 0.1%. PT: 10 sec., PIT: 28 sec. Coombs tests were negative. Urine was yellow and dipstick negative. EKG: sinus tachycardia with no evidence for ischemia. Bone marrow: Hypercellularity with full myeloid maturation but striking absence of red cell precursors. The patient was transfused to a hb of 11 gms/dl HIV test: strongly positive. CD4 and CD8 counts were 60 and 770, respectively. Chest x-ray, chest CT and chest MRI were negative for mediastinal mass. Abdominal CT demonstrated no lymphadenopathy or splenomegaly. Erythropoietin: 360 uM (normal < 60 20uM). Parvovirus B19 DNA titers: markedly elevated in acute and convalescent sera, consistent with ongoing parvoviral B19 infection. The impression was of pure red blood cell aplasia caused by parvovirus B19 infection presenting as the first manifestation of HIV disease in a homosexual male. The patient has remained RBC transfusion dependent with no evidence of reticulocytosis. He has been referred to the NHBLI for experimental immunoglobulin treatment as one of several newly described AIDS patients with parvoviral B19 induced pure RBC aplasia.

19. Infectious Mononucleosis in an Elderly Man

L. Miller, MD, Roger Williams General Hospital (State Univ NY, Stony Brook)

J. Forest-Lam, MD, Roger Williams General Hospital (Eastern Virginia)

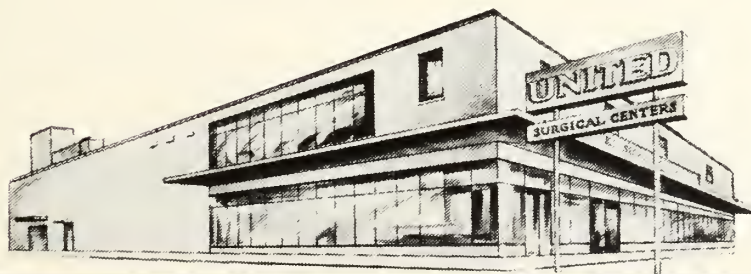
P. O'Dowd, MD, Clin Assistant Professor of Medicine.

A 79-year-old male was admitted with a 4-week history of anorexia, weight loss (8×2 weeks), fever (102°), nightsweats, cough and malaise. He had recently remarried. There had been a brief urticarial rash. There was a diffuse, moderate, firm adenopathy with hepatosplenomegaly. The lung, heart, abdominal, skin and joint exams were normal. Lab showed a significant lymphocytosis (WBC = 21K; 68% Lymph, 7 Atypical, 2 Plasmacytoid) and liver function abnormalities (ALK PHOS = 1100/280, SGOT = 94/40, SGPT = 99/40, T.BILI = 2.6, GG T = 525/50, LDH = 400/260). A lymphocytic malignancy was suspected. The large cell, granular morphology of the lymphocytes suggested T cell origin. A marrow was hypocellular showing increased large lymphs and plasma cells. There were occasional lymphohistiocytic aggregates suggestive of granulomata. Special stains for AFB and fungus were negative. Flow cytometry of blood and marrow identified the large lymphs in suppressor/cytotoxic subset. Serologies were positive for acute EB virus infection (Monoalert = IgG and IgM positive). The patient was discharged and followed. Over the next 3 months his symptoms, adenopathy and hepatosplenomegaly slowly resolved. His LFTs returned to normal. He has felt well for 6 months. The medical literature acknowledges that mononucleosis can occur in the "elderly." The most quoted paper, however, lists only one patient over the age of 70. This would appear to be an additional case.

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Cheating in Medical School: A Problem or an Annoyance?

Barry Stimmel, MD

... A subject that all too often is ignored to the detriment of the profession, the individual physician, and, most important, the patient.

It has always been somewhat puzzling how the public can consider physicians among the most ethical and respected of professionals, secondary only to members of the clergy, while regarding those who wish to enter into the study of medicine with a degree of derision unsurpassed by any other group of students. Premedical students have long been stereotyped as narrow-minded, competitive, backbiting, boorish individuals to be avoided at all costs.

What can be the process then that transforms this student, shunned by his/her undergraduate peers, into a compassionate, caring, and universally well-respected physician? Perhaps the easiest and most accurate response is that this is a far from accurate description of premedical students. Indeed, there is a

great heterogeneity among medical students, with the premedical stereotype being, in reality, the exception rather than the rule.

The effects that the curriculum or the faculty may have on medical students, however, should not be minimized. This may not always be salutary as it is equally true that many consider the basic science years of medical school to be far from an enlightening or humanistic experience but rather one which may foster the "premedical environment," emphasizing retention and regurgitation without creative thought or independent self-learning. Yet, while being goal-oriented, obsessive, and focused toward medicine, to the exclusion of other endeavors or life experiences, may not be considered optimal, this in and of itself is not necessarily worthy of derision and certainly is not unethical.

Unethical behavior has been noted in individuals long before they attend medical school and, unfortunately, exists throughout the educational process. Cheating appears to be prevalent in both secondary schools and colleges.

Such behavior has been found to exist independent of religious or moral attitudes or even of the desire to devote oneself to scholarly or altruistic activities, including the study of medicine.^{1,2} Many have ascribed the cheating seen in the premedical environment to the extreme competition in gaining admission to medical school. However, although this can never be an acceptable excuse, in fact, over the last decade, medicine has been one of the easiest graduate programs to enter, with virtually everyone accepted having the potential to graduate. Nevertheless, there is no evidence to suggest that cheating or other examples of unethical behavior at the premedical level has in any way diminished.

Once in medical school, although more than half of the schools use a non-ranking honors/pass/fail grading system, cheating is far from minimal. Approximately 25% to 60% of students reported cheating at least once in medical school and up to 57% of a group of students stated that they had been put at an unfair advantage as a result of

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other students' cheating.^{3,4,5,6} One might argue that cheating on a single examination does not indicate dishonesty with respect to pursuing a career in research or in the practice of medicine. However, evidence suggests that in both of these areas a considerable relationship exists between student cheating and subsequent inappropriate behavior. Sierles *et al* found a highly significant correlation between cheating and falsifying information about patient care ($P<001$) or reporting a normal finding on a patient without actually obtaining the information ($P<001$).⁴ A survey by Sheehan *et al* of a third year medical class found 27% of students claiming they had seen classmates cover up mistreatment of patients or engage in other unethical behavior, with 9% reporting they had witnessed classmates cheat in research.⁶

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Not surprisingly, the same study revealed 40% of students to have observed residents or interns cover up mistreatment of patients, with 3 out of every 10 students reporting having observed residents engage in unethical behavior or falsify information and 7% observing house staff cheat in research. The study did not document a decrease in such behavior once a physician became a member of the faculty. Twenty percent of students reported witnessing clinical faculty cover up mistreatment of patients or engage in other unethical behavior, with 8% of students observing clinical faculty falsify information

and 5% observing faculty cheat in research.

Of even greater concern is the observation suggesting that the number of students who cheat or engage in other unethical behavior increases from freshman to senior medical school year. Most discouraging is the observation that behavior clearly considered unethical by most cannot be recognized as such by some students, academicians, or practitioners.^{6,7,8} A study by Simpson *et al* of 683 medical students found that only 70% considered copying a lab report from a friend as inappropriate and only 38% considered signing an attendance sheet for a friend in the person's absence as something that should be prohibited.⁹ With respect to dishonest clinical behavior, only 64% of the students considered it inappropriate to change a diagnosis in order to increase hospitalization time, with significantly fewer senior students (46%) than freshmen (81%) actually judging this action inappropriate. Significantly fewer seniors, as compared to freshmen, considered it inappropriate to cover up for a classmate's failure to record patient care orders or to omit information from a patient's record in order to avoid a lawsuit. Fourteen percent of seniors believed that one had "to cheat sometimes to get ahead" as compared to 4% of freshmen. This suggests that although freshmen students appear to make judgments based on the conventional acceptance of society's mores, in fact, during exposure to house staff and attending physicians, these moral choices, rather than being strengthened through role modeling, diminish.

Equally important is the observation that even in the absence of unethical behavior on the part of one's self, both medical students and physicians are more likely

than not to refrain from reporting or confronting others whose behavior does not meet appropriate standards. Reuben and Noble, in a study of 76 internal medicine house officers, found that only 72% of residents would call to the attention of the chief resident an alcohol-impaired attending physician and only 50% an incompetent house officer.¹⁰ This observation is consistent with the public perception of a "conspiracy of silence" among physicians addressing areas of inappropriate behavior in their own profession.

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The institutional response to unethical and inappropriate behavior often is also far less than satisfactory. Curricular changes, such as deemphasizing the importance of examinations, using small group teaching, or introducing lectures and seminars on ethical issues, have never been shown to be effective in changing behavior. Deans and faculty frequently state formally that unethical behavior will not be tolerated, and, in most instances, guidelines concerning management of such allegations on the part of both medical students and faculty exist. However, such behavior is often implicitly condoned. Honor codes, existing in a number of medical schools are, in general, considered effective.¹¹ This perception, however, may not be accurate. Many medical students are against such codes. In those institutions where present, few identify violations. Brooks *et al*, in reviewing the effectiveness of a medical school honor

code, noted that although 76% of students indicated that it was an effective mechanism for handling students' suspected violations, only 6% of students who had identified a possible violation had actually reported this to the honor board.¹² A study by Sierles *et al*, comparing proctored with unproctored examinations in a school which created an honor system, found significantly more students cheated and observed others cheating in unproctored, compared to proctored, examinations.¹¹ Similar to earlier studies, of 17 students who observed cheating, only 2 reported it, with the offenders' names not provided in either case.

It is not uncommon for faculty to perceive their roles as educators rather than enforcers or maintainers of ethical standards. Indeed, faculty are often equally negligent in reporting suspected cases of unethical behavior or even impairment among house staff or peers. Many faculty have encountered instances of fabrication on the part of residents; however, follow-up of such behavior is relatively infrequent. Similarly, peer reporting of impaired colleagues is far from optimal. And, even with respect to allegations concerning fraud in research, faculty-institutional awareness has only recently begun to develop. In summary, unethical behavior on the part of medical students, house staff, and attendings, while not proven to be worse than that occurring in other professions, is not documentarily any better.

What can, if anything, be done to address this issue? It is quite true, as frequently stated by those of a more cynical bent, that unethical behavior does not become implanted as one enters medical school. It is equally correct that one who has cheated all of his/her life will continue to do

so throughout medical school and the subsequent practice of medicine. Unethical behavior is also not limited to any particular profession. However, those individuals hopefully comprise a relatively small proportion of any medical student or physician cohort. A larger number of this cohort includes those who will engage in unethical behavior if such behavior is perceived by them as being the norm or of relatively meaningless importance. And, perhaps, the largest proportion of students and physicians are those who do not engage in such behavior but, unfortunately, will do nothing to "stand up and be counted," indicating their intolerance of such behavior among their colleagues or teachers.

It is not uncommon for faculty to perceive their roles as educators rather than enforcers or maintainers of ethical standards.

There have been many studies to determine associations that tend to promote cheating. Those that have been identified are easy to understand.^{13, 14, 15, 16} They include: a) the presence of stressful conditions serving as deterrents to learning, accompanied by what is perceived as inappropriate methods of testing knowledge; b) the possibility of failure following initial success; c) the attitude on the part of students that faculty condone such activity; and d) the presence of unproctored, unstructured examinations. It is commonly assumed that most people who cheat do not need to do so. Although in the case of high achievers, such as medical students, this may be correct, it has also been documented that the need to achieve, regardless of capability, is positively associated with cheating.¹⁷ This sug-

gests that cheating is really independent of grade point average or aptitude. The level of achievement required, however, can well affect the amount of cheating, with students more likely to cheat when skills, rather than luck are needed. Regardless of the validity of these associations, there is no easy or simplistic way to eliminate cheating or other unethical behavior either at the medical student or the physician level. This, however, is not to suggest that something cannot or should not be done.

What is needed is a comprehensive approach, directed at both students and faculty, to: 1) sensitize all members of the academic community that the school will not tolerate unethical behavior, be it cheating on examinations, misreporting laboratory data, or misrepresenting research; 2) develop a better sense of awareness of the factors that promote or allow such behavior to continue; 3) develop a sense of responsibility so that members of the academic community will ignore neither peers nor teachers who engage in such behavior; 4) define quite clearly the steps to be taken to diminish this activity; and 5) develop a confidential method of reporting such activity to allow for appropriate identification while protecting due process.

There is neither a single nor a proven effective way to accomplish these objectives. However, on a faculty level, what seems most reasonable is the development of a series of ongoing workshops to address the issue of cheating among students and unethical behavior among peers. Testing should be conducted under conditions that do not encourage cheating. With multiple choice examinations, computer programs similar to those used by the National Board of Medical Ex-

aminers to detect cheating should be instituted. Faculty must be held accountable for their behavior in the classroom, on the clinical services, and when providing evaluations of students. With regard to students, commencing with the first year of medical school and continuing for the entire 4 years, a system should be developed to allow for ongoing discussion groups dealing with ethical issues inherent in the practice of medicine. Such groups should be relatively small in number of members and should be led by senior clinicians who provide excellent role modeling. There should be frank discussions concerning questionable behavior as well as ways of dealing with such behavior in others. By maintaining group continuity, solidarity may develop that will allow for thoughtful action. Whether such responses will actually diminish cheating in medical school or subsequent inappropriate behavior as house staff or physician is, of course, impossible to predict as, unfortunately, it has been demonstrated that positive thoughts concerning moral behavior and one's subsequent actions are not necessarily correlated.^{18, 19} However, at the least, this paper may bring to the surface a subject that all too often is ignored to the detriment of the profession, the individual physician, and, most important, the patient.

References

- ¹ Baird JS. Current trends in college cheating. *Psychol in the Schools* 1980;17(4):515-522.
- ² Smith RE, Wheeler G, Diener E. Faith without works: Jesus people, resistance to temptation, and altruism. *J Applied Social Psychol* 1975;5(4):320-330.
- ³ Stimmel B, Yens D. Cheating by medical students on examinations. *Am J Med* 1982;73:160-164.
- ⁴ Sierles F, Hendrick I, Circle S. Cheating in medical school. *J Med Educ* 1980;55:124-125.
- ⁵ Cockayne TW, Samuelson CO Jr. The crime and punishment of cheating in medical school. *Research in Medical Education*; 1983

Proceedings of the Twenty-Second Annual Conference, pp 166-171. Association of American Medical Colleges Annual Meeting, Washington, DC, 1983.

- ⁶ Sheehan KH, Sheehan DV, White K, Leibowitz A, Baldwin DC, Jr. A pilot study of medical student abuse. *JAMA* 1990;263:533-537.
- ⁷ Wolk DJ. Student doctors: Learning to lie. In: *Health and Human Values, Winning Essays of the Essay Contests for Students in the Health Professions*. Hastings on Hudson, New York: Society for Health and Human Values, 1980.
- ⁸ Petersdorf RG. A matter of integrity. *Acad Med* 1989;64:119-123.
- ⁹ Simpson DE, Yindra KJ, Towne JB, Rosenfeld PS. Medical students' perceptions of cheating. *Acad Med* 1989;64(4):221-222.
- ¹⁰ Reuben DB, Noble S. House officer responses to impaired physicians. *JAMA* 1990;263:958-960.
- ¹¹ Sierles FS, Kushner BD, Krause PB. A controlled experiment with a medical student honor system. *J Med Educ* 1988; 63:705-712.
- ¹² Brooks CM, Cunningham R, Hinson N, Browns Weaver B. Student attitudes toward a medical school honor code. *J Med Educ* 1981;56:669-671.
- ¹³ Vallacher RR, Solodky M. Objective self-awareness, standards of evaluation, and

moral behavior. *J Exp Social Psychol* 1979;15(3):254-262.

- ¹⁴ Karabenick SA, Stuart A, Srull TK. Effects of personality and situational variation in locus of control on cheating: Determinants of the congruence effect. *J Personality* 1978;46(1):72-95.
- ¹⁵ Houston JP, Ziff T. Effects of success and failure on cheating behavior. *J Educational Psychol* 1976;68(3):371-376.
- ¹⁶ Houston JP. Learning and cheating as a function of study phase distraction. *J Educ Research* 1976;69(7):247-249.
- ¹⁷ Johnson PB. Achievement, motivation and success: Does the end justify the means? *J Personality and Social Psychol* 1981;40:374-375.
- ¹⁸ Blasi A. Bridging moral cognition and moral action: A critical review of the literature. *Psychological Bulletin* 1980;88:1-45.
- ¹⁹ Monte CF, Fish JM. Lying true: An investigation of moral inconsistency in unethical behavior. *Internat J Group Tensions* 1980;10:130-138.

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30	\$ 4.66	\$11.65	\$ 23.30
35	\$ 7.33	\$18.35	\$ 35.07
40	\$13.21	\$20.13	\$ 35.94
45	\$15.68	\$23.58	\$ 42.43
50	\$17.86	\$33.34	\$ 62.35
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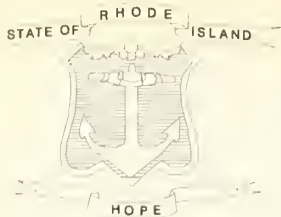
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Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

An Outbreak of Staphylococcal Food Poisoning among East Providence School Children

Staphylococcal food poisoning is the second most commonly reported cause of acute food poisoning in the United States, after salmonella. It accounts annually for 20% of all outbreaks involving contaminated food. The disease results from the ingestion of a heat-stable enterotoxin which is preformed by a toxigenic strain of *S. aureus* growing in a contaminated food. A number of foods promote the growth of *S. aureus*; the most common are custard-filled pastries, canned food, processed meats, potato salad, and ice cream.¹

On May 31, 1990, the Rhode Island Department of Health was notified of the sudden onset of nausea and vomiting among students at two elementary schools in East Providence. The school superintendent reported that the children had become ill several hours after eating the school lunch, which consisted of sliced ham, baked beans, corn, bread and butter, and pudding. The food had been prepared at one school and was subsequently distributed to four additional schools.

For 662 lunches served there were 100 reported illnesses, yielding an attack rate of 15% for all 5 schools combined. Two schools made up the bulk of the cases, however, with School A reporting an attack rate of 47% (67/144) and School B reporting an attack rate of 18% (27/153). Attack rates at each of the remaining 3 schools C, D, and E were each less than 5%.

Telephone and in-person interviews eliciting symptom and food histories were conducted the following day. Interviews were completed with 134 (93%) of 144 students enrolled at School A. Among 65 ill students interviewed, complaints of

nausea (90%), vomiting (81%) and cramps (66%) predominated with a median incubation period of 2.8 hours (Figure 1). The risk of illness associated with the consumption of each food item was calculated. The relative risk associated with the consumption of ham was 17.7 (95% CI = 2.6, 122.0) whereas for the rest of the food items, relative risks ranged from 0.8 to 1.6 (Table 1). A dose response relationship was observed between the amount of ham consumed and the risk of illness: the relative risk for consumption of more than 2 slices of ham was 21.5 (Table 2).

Samples of food and vomitus were analyzed for the presence of *S. aureus*, which was found in each sample in large amounts (> 2,000,000 organisms/gm food). (Pre-formed staphylococcal enterotoxin A was also detected in the food sample submitted to the Food and Drug Administration.) In addition, 8 food handlers submitted to nasal and pharyngeal cultures for *S. aureus*. One food handler was positive. Subcultures of isolates from the positive food handler as well as from 19 samples of food, stool, or vomitus revealed identical phage patterns and plasmid profiles. The food handler in question reported peeling the inner casing off only 2 out of 9 still-warm hams prior to their slicing, providing a potential explanation as to why the outbreak was confined largely to 2 of 5 schools. Food Protection inspectors found evidence of excessive handling and improper cooling of the pre-cooked ham. It was concluded that the culture positive food handler introduced *S. aureus* to the ham rolls while removing the casings, and that the *S. aureus* had ample opportunity

to multiply and to elaborate toxin during subsequent handling.

¹Waldvogel, FA: *Staphylococcus aureus* (including Toxic Shock Syndrome), in Mandell GC, Douglas RG, Bennett JE (eds): *Principles and Practice of Infectious Diseases*. New York, Churchill Livingstone Inc., 1990.

Figure 1: Number of Hours from Eating Lunch to Onset of Illness

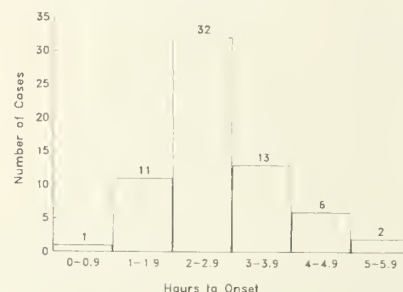


Table 1: Risk of Illness Associated with Consumption of Specific Food Items, School A

Food Item	Relative Risk	95% Confidence Interval
Ham	17.7	2.6-122.0
Baked Beans	1.6	1.1-2.2
Milk	1.4	0.7-2.9
Van. Pudding	1.4	0.7-3.0
Corn	1.2	0.9-1.7
Bread & Butter	1.1	0.8-1.7
Choc. Pudding	0.8	0.5-1.1

Table 2: Risk of Illness and Amount of Ham Consumed, School A

Amount of Ham Eaten	Total	Number Ill	Attack Rate	Relative Risk	95% Confidence Interval
none	28	1	4	1.0	(referent)
< 2 slices	20	4	20	5.6	0.7-46.4
2 slices	34	20	59	16.5	2.4-115.2
> 2 slices	52	40	77	21.5	3.1-148.5
Total	134	65			

Submitted by the Office of Disease Control, Epidemiology and Communicable Diseases Division, Barbara A. DeBuono, MD MPH, Medical Director, Thomas T. Gilbert, MD MPH, Margaret S. Richards, PHD, and Marilyn Rittman, RN.

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with May 1990	
	May 1990 Number	Number	Rates
Live Births	1,286	15,784	15.8*
Deaths	815	9,740	9.8*
Infant deaths	(11)	(152)	9.6†
Neonatal deaths	(6)	(123)	7.8†
Marriages	887	8,196	8.2*
Divorces	374	3,748	3.8*
Induced Terminations	654	7,816	495.2†
Spontaneous Fetal Deaths	100	1,190	75.4†
Under 20 weeks' gestation	(91)	(1,088)	68.9†
20 + weeks' gestation	(9)	(95)	6.0†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with February 1990		
	February 1990 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	292	3,448	345.5	4,536.0
Malignant Neoplasms	159	2,421	242.6	6,501.5
Cerebrovascular Diseases	46	584	58.5	802.5
Injuries (Accident, Suicide, Homicide)	31	443	44.4	10,248.5
COPD	33	331	33.2	458.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 998,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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Standards of Medical Care for Diabetic Patients: A Panel Discussion

Stephen F. Quevedo, MD (moderator)
Charles B. Kahn, MD,
Tom J. Wachtel, MD

"The concept that controlling diabetes mellitus makes a difference in the outcome of diabetic patients is a major principle behind the formulation of standards of care."

The following is an edited transcript of Medical Grand Rounds at The Miriam Hospital held on October 26, 1989.

DR. QUEVEDO: We have assembled a panel of distinguished physicians to help guide us through a controversial document, the Standards of Care article that ap-

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Tom J. Wachtel, MD, is Associate Director of the Division of General Internal Medicine, Rhode Island Hospital and Associate Professor of Community Health at Brown University, Providence, Rhode Island.

peared in the May 1989 issue of *Diabetes Care*.^{1,2} Dr Charles Kahn is a physician in the private practice of diabetes and endocrinology and Associate Clinical Professor of Medicine in the Brown University Program of Medicine. Dr Tom Wachtel is Associate Director of the Division of General Internal Medicine at Rhode Island Hospital and Associate Professor of Community Health at the Brown University Program of Medicine. He is a clinical epidemiologist.

By the late 1980s third party payers had expressed a clear interest in how we practice medicine. At the same time, the American Diabetes Association (ADA) continued to be concerned with improving the quality of care of diabetics throughout the country. The ADA board commissioned its Committee on Professional Practice to develop a standard of care that could be utilized nationwide. This group, composed of nine physicians, predominantly academic diabetologists and subspecialists, a PhD nutritionist, a nurse-educator, a lawyers, and an epidemiologist, published the standards of care document in the May 1989 issue of *Diabetes Care*. The September issue of *Diabetes Forecast*, the ADA patient publi-

cation, contains an article outlining the standards.³

In addition, a recent article in *Diabetes Spectrum* attempts to explore the thinking of the panel, and examine some of the ensuing controversies.⁴ The ADA is also sponsoring a nationwide clinical education program (CEP) for physicians in March, 1990. This program uses the standards of care as the backbone of a very focused education program, and indeed Dr Charles Kahn on our panel will be involved as faculty.

What I'd like to do initially is

ABBREVIATIONS USED:

ADA: American Diabetes Association

CEP: Clinical Education Program

DCCT: Diabetes Control and Complications Trial

EKG (ECG): Electrocardiogram

HDL: High density lipoprotein

HMO: Health Maintenance Organization

NIH: National Institutes of Health

PTCA: Percutaneous Transluminal Coronary Angioplasty

UGDP: University Group Diabetes Program

ask our panel to discuss some general issues. We will have Dr Kahn speak first to review some of the data in the medical literature supporting diabetic control, and then have Dr Wachtel discuss practice guidelines. What does controlled diabetes do for the patient?

DR KAHN: I am most happy to discuss the subject of standards of care in diabetes mellitus. For purposes of discussion we are talking about type I and type II diabetes mellitus, with general standards of care relating to both. The basic purpose in developing standards of care is to provide general guidelines for all physicians taking care of diabetic patients, particularly the general practicing physician. The board certified endocrinologist/diabetologist would be involved in working with the general physician in a consultative, collaborative way and probably more directly in the care of the more difficult diabetic patients.

The concept that controlling diabetes mellitus makes a difference in the outcome of diabetic patients is a major principle behind the formulation of standards of care. There is little argument that sufficient daily control of diabetes, to avoid symptoms, is warranted. The idea that controlling diabetes mellitus, over time, has an advantageous impact upon the long-term outcome of the diabetic patient remains a less clear issue. There are a number of prospective and retrospective clinical studies which strongly suggest that control of diabetes does make an important difference. The Joslin Clinic experience⁵ and the Iowa study⁶ represent some of the more important retrospective studies. The Kroc collaborative studies,⁷ studies carried out at Oxford in the United Kingdom,⁸ Pirart's study,⁹ and those carried out in Texas¹⁰ represent some of

the prospective data that correlate control with complications.

The UGDP trial¹¹ was the only negative prospective study, but this report has been quite controversial and had not been fully accepted. The most interesting prospective study of tight diabetic control is now being carried out in the United States and Canada. The Diabetes Control and Complication Trial (DCCT)¹² is comparing tight diabetic control using insulin pumps or multiple injection programs with more standard, conventional insulin therapy. This is an 8-year prospective trial, and data are not yet available, since the study has 4 more years until its conclusion.

There are studies of secondary diabetes in man¹³ and secondary diabetes in experimental laboratory animals,^{14, 15} which add further evidence that the metabolic derangement of diabetes plays a major role in development of diabetic complications. How directly applicable these studies are to type I or type II diabetes mellitus remain less clear. A growing volume of data suggest that the metabolic derangement of diabetes is a major factor in the development of these degenerative complications, and therein lies the issue about control. When I discussed the subject of control and complications in the past, I had developed three learning objectives. First, that the data suggest that the metabolic derangements are a principal factor in the development of the chronic degenerative complications of diabetes; second, very much related to the purpose of standards of care of diabetes mellitus, is that good control of diabetes is achievable with diet, oral agents, or insulin therapy. Given the first two objectives, the third is that good control of diabetes will have a favorable impact upon the development of and/or progression of

the chronic degenerative complications of diabetes.

DR QUEVEDO: When you mention degenerative complications,

“Macrovascular disease, such as atherosclerotic peripheral vascular, coronary vascular, cerebral vascular, and renal vascular disease, occurring with increased incidence in type II and type I diabetes, may not respond as favorably to control . . .”

you are specifically talking about microvascular complications rather than macrovascular complications, are you not?

DR KAHN: Yes. Obviously, the statement was more directed towards microvascular retinal disease and nephropathy, a glomerular microvascular disease. Neuropathy is not a direct example of microvascular disease, but we consider it as one of the more specific complications.

Macrovascular disease, such as atherosclerotic peripheral vascular, coronary vascular, cerebral vascular, and renal vascular disease, occurring with increased incidence in type II and type I diabetes, may not respond as favorably to control, which is an area of much current research.

DR WACHTEL: Practice guidelines are standardized specifications for care, either for the use of a particular procedure or for the management of a specific clinical problem.

Guidelines are nothing new; they have been used for years: For example, protocols for diagnosis and management of cancer, recommendations for the use of screening tests such as the Pap smear, or mammography, recommendations for vaccination or

manuals for diagnosis and treatment (for example, of hypertension or hypercholesterolemia). Furthermore, many physicians' minds seem to function as if some implicit guidelines were being followed for decision-making. So what's all the recent fuss about practice guidelines?

The concern is that formalization and widespread dissemination of guidelines infringe on the physician's independence, and we don't like that. If guidelines have been around for a long time, mainly for the sake of quality, what's happened to bring them to the forefront in the past few years? The answer is cost containment. The third party payers, I believe, are going to develop practice guidelines and use them as guidelines for reimbursement. Again, I don't like that, but the payers are convinced that doctors are ordering tests, procedures and treatments that are not necessary, and they are determined to stop paying for the unnecessary items.¹⁶

The response of the American College of Cardiology, for example, was to create a task force on assessment of diagnostic and therapeutic cardiovascular procedures, sponsored both by the Health Care Financing Agency and by the American College of Physicians, producing a number of fascicles published in the *American Journal of Cardiology*. I have here, for example, the "Guideline for Coronary Angiography,"¹⁷ "Guideline for PTCA,"¹⁸ and "Guidelines for Ambulatory Electrocardiography."¹⁹ There are many of these already published and we are going to see more. The American Society of Gastroenterology is doing the same thing for endoscopy. I think this is the response that all of organized medicine should make to payers and planners. Physicians should decide what is appropriate care

and what is not, not the third party. Practice guidelines which are flexible enough to allow physicians to meet their patient's individual needs are the way to go in the present climate.

Now, what should guidelines

"The third party payers . . . are going to develop practice guidelines and use them as guidelines for reimbursement."

be?²⁰ First, guidelines can be developed for use of a procedure or for the management of a clinical problem. They must be comprehensive. All situations should be considered. They must be specific, clearly defining the clinical situation. They must be detailed enough to distinguish features that separate one indication from another. They should clearly indicate what is appropriate and what is not. Finally, and this is probably the most important point, they must be manageable.

Who should develop guidelines? Some national organizations have taken the lead in setting up consensus panels, for example, the American College of Cardiology, the NIH, and the American Diabetes Association. However, my personal bias is that local groups of physicians with a common interest or practicing in a common organizational framework such as a hospital staff or an HMO should reformulate existing guidelines or create new ones where none exist. At Rhode Island Hospital, for example, we are in the process of creating guidelines for the management of specific clinical problems on a hospital-wide basis. We have selected clinical problems based on their prevalence, the relative predictability of the hospital course, and, of course, the cost of the

hospital stay. We're particularly interested at this point in developing guidelines for outliers.

The NIH, on the other hand, selects problems that are major public health issues, such as hypertension²¹ or hyperlipidemia²³. Guidelines for procedures are somewhat easier to deal with and are ideally suited to address such problems as unnecessary surgery or unnecessary invasive procedures. This type of guideline is most useful for procedures that have potential for harm, procedures involving extensive use of resources, procedures that are controversial or in part outdated, or procedures suspected of overuse or inappropriate use.

Aside from the threat to our independence, what are legitimate concerns about the use of practice guidelines?²³ The first concern is quality of care. I think that guidelines actually define the process of care. In order to evaluate quality of care, one can either look at the *process* of care or the *outcome* of care. Guidelines clearly have nothing to do with outcome, but they define the process of care, and insofar as they represent reasonable care, they insure that acceptable quality of care is preserved. Quality assessments are, in fact, facilitated since physicians manage their patients according to preset criteria.

The second issue concerns the physician-patient relationship, which should not be affected by the provision of standardized care that is designed to provide management with the best risk-benefit ratio. Again, there must be an inherent flexibility allowing physicians to meet individual patient needs.

Third, and certainly not the least, is the fear of litigation. This could be alleviated by the reassurance to physicians that their

peers in the community are practicing according to the same guidelines. The flip side of this is that deviation from the standards would be easier to detect by lawyers or patients and perhaps more difficult to defend in court; this is a legitimate concern.

"... my personal bias is that local groups of physicians with a common interest or practicing in a common organizational framework such as a hospital staff or an HMO should reformulate existing guidelines or create new ones where none exist."

Fourth, relationships with colleagues may, in fact, be enhanced by the ongoing need to review, discuss, and update the guidelines, especially if they're implemented and created at a local level such as a hospital staff.

Fifth, income would not be adversely impacted for most physicians. Guidelines may affect those few physicians whose income is dependent on the provision of unnecessary services. I don't have a problem with that.

Finally, reallocation of resources should not affect the patient. At the institutional level or at the regional or national health planning level, some readjustments might be implemented; for example, if a procedure or piece of equipment becomes outdated. A real danger, I think, is for third parties to abuse the guidelines by imposing inflexible adherence for reimbursement.

DR QUEVEDO: I'd like now to go through the standards. One of the recurrent themes that certainly I will bring forth is something that Dr Wachtel has mentioned, namely the desirable flexibility in a *guideline* is not

here. This is a rigid *standard* of care. The opening statement states that the patients should get their care from physicians with "expertise and a special interest in diabetes." Does that mean every patient with diabetes needs to see a board certified diabetologist/endocrinologist?

Dr Bruce Zimmerman from the ADA Committee for Professional Practice is on record as saying that, "It should be an interested, knowledgeable physician," implying that he/she does not have to be solely a board certified diabetologist/endocrinologist caring for these patients. Any competent internist, osteopath or family practitioner who is interested in taking care of diabetic patients, and delivers quality care by keeping up to date is capable in the view of the ADA.

DR KAHN: That is the purpose of the ADA-CEP course. We welcome endocrinologists and diabetologists, but we are primarily targeting the general practicing physician interested in caring for the diabetic patient.

DR QUEVEDO: The first section of the document covers the initial visit. In terms of the medical history, it is self-explanatory and detailed. From a public health perspective special attention needs to be paid to risk factors for atherosclerosis. In most cases, diabetic patients die of macrovascular complications, and you have probably done much more good by getting a diabetic patient to stop cigarette smoking than if you drop his fasting blood sugar by 10 mg/dl.

Regarding the physical examination, a very provocative article published this year looked very critically at what we benefit by doing a comprehensive yearly physical examination.²⁴ It was interesting to see how little of what we do as part of a "yearly examination" has been shown to be of

proven value.

DR WACHTEL: I would like to say something about that. I have a problem with that paper because of its narrow viewpoint. Failing to show that something is effective is not equivalent to saying that something is ineffective, and while it may be true that listening to somebody's lungs on an annual basis does no clear good, I do not see how it could possibly do any harm. We all examine patients, and I presume that we will continue to do this. The paper accomplishes nothing except perhaps to set the stage for research to determine which parts of the physical exam are most effective.

DR QUEVEDO: That paper makes us think about what we do so we can practice in a cost-effective and intelligent fashion. I think this article generated a lot of discussion.

DR KAHN: Again, we are dealing not with a healthy population, but with patients with a chronic disease that has identifiable complications. I do examine the patient but I specifically focus on certain parts of the physical examination, such as looking in the eyes, evaluating the circulation, screening for hypertension and checking the neurologic status because these are high yield areas in diabetic patients.

DR QUEVEDO: In terms of the suggested physical exam, most of that again is fairly straight forward. We will soon get to the ophthalmology screening controversy, but should the primary care provider do a dilated pupil exam if the patient is going to be seen by someone with more expertise anyway?

DR KAHN: No. I would suggest that your examining room be as dark as possible, and that you give the eyes a chance to accommodate a bit to enhance your exam.

DR QUEVEDO: I know there's some controversy in the labora-

tory section. They recommend a random sugar or a fasting sugar, glycosylated hemoglobin, a complete fasting lipid profile, thyroid function studies (this generated controversy in committee), and a urine evaluation, if available, by a microalbuminuric method.

"From a public health perspective special attention needs to be paid to risk factors for atherosclerosis."

DR WACHTEL: I have a strong preference for fasting plasma glucose in type II diabetes.²⁵ A random blood sugar doesn't tell me a whole lot, so I would rather not do it. If at all possible, I would prefer to check fasting glucose levels. I do not believe that a glycosylated hemoglobin is indicated at the time of the initial exam. It is going to be high if the patient has a high blood sugar. My sense is that the primary purpose of the glycosylated hemoglobin is to determine if indeed a patient you thought was well controlled by home glucose monitoring truly is, in fact, well controlled. As far as lipid profiles, I do the same for diabetic persons as I do for the population at large: I start with total cholesterol. If it is higher than 200 mg/dl then I fractionate for triglycerides and HDL. Serum creatinine is good to get as a baseline in all diabetic persons. I get a urinalysis. If there is no proteinuria on the dipstick, I don't go beyond that. I order a urine culture if the microscopic examination is abnormal, or if the patient has symptoms of an infection. I'm neutral on thyroid function testing, and an ECG is indeed useful to obtain as a baseline, but not on an annual basis.

DR KAHN: Fasting plasma glucose, I think, is a most useful test, especially in those type II diabetics on diet or oral agents, but

it is to some extent impractical. In our office we do random glucose determinations whenever the patient is seen. Arranging for fasting blood glucose determination would be most difficult and would usually separate in time the glucose determination and the office visit. More importantly, the majority of patients, especially those on insulin, are doing some kind of standardized home glucose monitoring. Under these circumstances I can complement the random office glucose with data, including fasting values, obtained at home. Obviously some means of determining the accuracy of home glucose monitoring is most critical.

The glycosylated hemoglobin is an important test in diabetes medicine. Emphasis on this test will be increasing rather than decreasing. It is becoming one of the most important pieces of information that helps in the complex determination of how a diabetic patient is doing clinically. The glycosylated hemoglobin is a retrospective evaluation of diabetic control over the previous 6 to 8 weeks.

A urinalysis 1 to 3 times a year is an important test to carry out in diabetic patients. The usual laboratory dipstick becomes positive when the urine excretion of protein is between 150 and 200 mg/dl, and represents the macrodetermination of urinary protein excretion. The issue of special testing for microalbumin excretion is less clear.²⁶⁻³⁸ There is some exciting information in the literature indicating that the earliest phase of diabetic renal involvement includes two identifiable features. First is an elevated creatinine clearance (so-called hyperfiltration) and the second the very earliest determination of increased urinary protein excretion above the usual 15 ug/min (200 mg/day) range which is consid-

ered normal. This is a determination carried out by radioimmunoassay for the microexcretion of albumin. At the present time this is best done on a 24-hour urine collection, which can be cumbersome. I think that some type of urinary microalbumin determination will be important in the future, since there are data indicating that when microalbuminuria is noted, tightening diabetic control, lowering dietary protein intake and perhaps lowering the blood pressure will have a positive impact on the future renal status of that patient. When I say lowering the blood pressure an area of controversy immediately arises. Most all would agree that controlling hypertension is indicated. However, there are those who now suggest that the blood pressure in a patient with microalbuminuria, or for that matter macroalbuminuria, should not exceed 120/80. Due to the complexity of the testing, I do not think that determining creatinine clearances in order to identify hyperfiltration is necessary for management of diabetic patients at the present time. Urine cultures are clearly indicated when clinical signs or symptoms and the urinalysis suggest a urinary tract infection.

Thyroid function testing is a most interesting subject. We had a negative interaction with local third party carriers concerning the medical necessity of thyroid function testing in any diabetic patient. Many physicians, including our practice, have felt that thyroid testing is an important part of the evaluation of type I diabetic patients. There are many articles in the literature showing that the prevalence of thyroid disease is as high as 25% in type I diabetics. The association may be secondary to a polyendocrinologic immune disorder. An initial thyroid function test in type I diabetics

and perhaps every 3 to 5 years thereafter is reasonable. In type II diabetics, where the prevalence of thyroid disease is increased, but to a lesser degree, such guidelines are less clear. Thyroid function testing might be better based upon pertinent associated clinical signs or symptoms in these patients.

The electrocardiogram (EKG) is an important test to perform initially. The timing of repeat testing is dependent upon a number of factors such as duration of diabetes, associated cardiovascular risk factors, other clinical information obtained at the time of the office visit and the baseline EKG. Diabetic patients of more than 20 year's duration can have unexpected, silent findings on EKG. The area of cardiac autonomic neuropathy is now being actively explored, and may eventually change the indication for obtaining the EKG.

DR QUEVEDO: The thyroid function test issue generated a lot of discussion in committee, and when it was sent out for review, specifically in type II diabetes, many reviewers claimed that the yield did not justify testing. In type I diabetes, the situation is different.

Let us now move on to the management plan. There are several important points to make from a public health perspective. The committee, by stating that ophthalmopathy screening be done by an "eye doctor," side-stepped a raging controversy regarding who should screen for diabetic retinopathy. As many of you know, there is an ongoing discussion between optometrists and ophthalmologists as to whether or not the former are qualified to do diabetic screening. The feeling of the committee is that in some areas of the country, optometrists are more readily available, and that the younger "better trained" optometrists may be per-

fectly capable of doing the screening, but then once an abnormality is found, patients should be referred to an ophthalmologist. This is an ongoing discussion and we will be hearing more about this in the future.

The care of diabetic women of childbearing age, which is my own area of interest, requires special consideration. It is important to discuss contraception, and introduce the concept of a planned pregnancy. Good control of mean blood sugar at conception and during the first 7 weeks of pregnancy (when most congenital malformations occur) is extremely important, and here is an instance where the glycosylated hemoglobin test is invaluable in ascertaining whether or not the patient is in adequate control, and when attempts to conceive may start. Studies in the obstetrics literature have clearly shown that normalizing or near normalizing glycosylated hemoglobins during this critical period can reduce greatly the excess incidence of malformations in type I diabetics.

DR WACHTEL: I believe that type I diabetics and insulin treated type II diabetics should be self-monitoring their blood sugar, not their urines. For type IIs on oral agents, I guess urine values are satisfactory, but patients on insulin should be monitoring their blood.

DR QUEVEDO: The continuing care section outlines very specific recommendations and is probably one of the most controversial parts of this document. When you should routinely see the patient, and how often you should see the patient after a change in their therapeutic regimen is outlined here in a very detailed fashion. I know it is quite controversial and I know you both wanted to comment about this.

DR KAHN: I think this is an area where we as a group, both general practice doctors and those

specializing in diabetology, have to maintain a certain degree of leeway. Rather than a specific guideline, I would rather say that it is appropriate to see the stable patient perhaps twice a year. I do not know that we have to specify an interval; after any change in the therapeutic program, a follow-up visit is appropriate. To see someone every 2 to 4 weeks throughout the year without changes occurring is abuse, and I think we need to be aware of that potential. We have to be very careful defining the exact nature of the follow-up because as the patient's physician we have to be in charge of those decisions which we are most comfortable with, and we need to be ready to defend our position.

"The care of diabetic women of childbearing age . . . requires special consideration. It is important to discuss contraception and introduce the concept of a planned pregnancy."

DR WACHTEL: I agree. I think the committee's suggestion that patients may need to be seen as often as daily is not often true. Even when you initiate treatment with insulin, you do not necessarily have to change the dose on a daily basis.

DR KAHN: But it allows somebody in a special circumstance to do it daily. We can all say it is probably not necessary, but rarely you are going to have the patient who should be seen daily for 3 or 4 days.

DR QUEVEDO: Also, in a setting like mine where we take care of gestational diabetic women and often start insulin in an out-patient setting, certainly, they are seeing me or the nurse practitioners daily for a period of time. Again, flexibility is what we seek. The ADA document, in this part

especially, comes across in a too rigid format.

DR WACHTEL: The same applies to weekly visits with the patients on oral agents. I tend not to see them that frequently even when I am changing dosages or therapeutic agents.

DR QUEVEDO: In terms of continuing care, interim history is discussed. A comprehensive examination is recommended annually, along with complete eye exams. I think all of us would certainly agree. With regards to the laboratory, again some of the controversy we have already touched upon comes to the fore here. A complete lipid profile, meaning triglycerides, total cholesterol, and HDL annually in adults is wasteful, specifically if patients are starting off with a normal profile. How do both of you feel?

DR KAHN: In nondiabetics, it's recommended every five years in an adult, as I recall. I think in a diabetic patient who is well controlled, and then has a normal initial lipid profile, I do not know what the answer is, but every other year if not every third year is fine. I think more often than every five years is appropriate, but I agree that annually is unnecessary.

DR WACHTEL: In addition to that, what I tend to do is begin with simple total cholesterol, and if the patient's total cholesterol is, for example, 150 mg/dl I am not interested in lipid fractions.

DR KAHN: You are not concerned about triglyceride as a risk factor?

DR WACHTEL: No, the state of the art doesn't suggest that triglycerides are that significant. I would be interested in Dr Herbert's thoughts on this.

DR PETER HERBERT (Director-Division of Nutrition and Metabolism, The Miriam Hospital): If you want to screen and identify abnormalities typical of diabetes, you need to check triglycerides

and HDL. One argument against screening is whether you should screen for something you can not readily correct, and that is a very open question. If physicians are unwilling or unprepared to initiate treatment if they find something abnormal on a test, then you can question the wisdom of testing in the first place. There is good evidence that most of the abnormalities in lipids that occur in diabetic patients respond to control of the diabetes, so it is another index of how well you are doing.

DR KAHN: One of the offsetting things also, if you are adding up risk factors, is that a low HDL in and of itself is a risk factor.

DR QUEVEDO: They recommend a protein excretion determination yearly, if possible by a microalbuminuric method; again, another very controversial area. There are many problems with the albumin excretion rate determination. On the one hand, they can vary seemingly spontaneously, with physical exercise during the collection period, fever, and with other intercurrent illnesses. On the other hand, if consistently elevated they are a marker for the development of significant proteinuria, and even perhaps a marker of long-term morbidity. The issue of screening and what to do with elevated excretion, if found, came up at the Newport Diabetes Symposium last May. I informally polled several of the symposium faculty, and came away with a feeling that patients should not be screened routinely at present. However, patients in whom perhaps you are looking for a reason to intervene because of mild hypertension, at levels of blood pressure where you would not necessarily treat a nondiabetic (ie, diastolic pressures in the mid to high 80s), and if you then found albumin excretion rates above normal, you might wish to start antihypertensive therapy. Again, it is soft data thus

far. There is also new epidemiological data that suggest there is a racial difference in the development of nephropathy. In a recent study from Michigan,²⁹ blacks were found to progress to significant nephropathy at a different rate than whites, but again looking back at it, the diastolic pressures of the black population were slightly higher than whites.

DR KAHN: I think this is where the ADA is ahead of itself. I would not recommend microalbumin determinations at the present time, but I think it is going to be the next step. I do not think we understand its role yet, I do not think we understand its validity yet; for example, how often do you do it? Do you need an average over 3 days? I would do it selectively in certain patients, but would routinely do a urinalysis for protein excretion. Practicing physicians for now should defer routine use of microalbumin determinations until more data accumulate.

DR QUEVEDO: The management plan speaks for itself. In the area of Special Considerations I know there are a couple of questions.

DR WACHTEL: Actually, I have several problems with that area. The first thing that shocked me was in the treatment of diabetic ketoacidosis and hyperosmolar coma in the physician's office. I have yet to encounter a patient with either of those complications that I am willing to treat on an ambulatory basis. Perhaps they are referring to patients who have not eaten in 2 days and are mildly ketotic, but I would not call those episodes diabetic ketoacidosis anyway. I think there is some evidence that there are specific risk factors for the hyperosmolar coma and probably the same for DKA; I think we need to be particularly aggressive in treating any infection, bacterial or viral, in diabetic persons. Older age is a risk factor

for hyperosmolar coma, and we need to be somewhat more careful monitoring the elderly diabetic. Nursing home residents also appear to be at higher risk.

DR QUEVEDO: There is another controversial area concerning nephropathy. The ADA suggests that the patient with abnormal renal function, proteinuria or elevated serum creatinine *requires* consultation with a specialist in diabetic renal disease. Now, if they take that to mean that every patient with microalbuminuria, for example, or minimal proteinuria needs to see a nephrologist, many of us will have misgivings. If a patient has a decreased creatinine clearance and/or troublesome hypertension, then the additional expertise of a nephrologist may be in the best interest of the patient.

DR KAHN: If we are doing our job in monitoring protein intake, monitoring the blood pressure, and the creatinine is normal, I think it is unnecessary to seek the advice of a nephrologist, unless something extraordinary is happening with the volume of protein excretion.

DR QUEVEDO: We are coming to a close now, and I would just like to share with you one of the concerns we had about the standards. What are some of the legal implications? I was fortunate enough to get an opinion from Mr Thomas Gidley, a well known malpractice defense lawyer in the State of Rhode Island. He has been kind enough to allow us to paraphrase him. He feels that standards like this are going to be admissible as court evidence in malpractice cases. However, and again this gets back to the theme of this discussion, he believes that

local groups, ADA affiliates, medical societies, specialty groups, hospital groups, indeed any group of practitioners can and should go on public record with reservations, modifications, and/or disagreements with such published standards. This is what we need to do in the coming years when we find ourselves confronted with standards, such as these, with which we do not necessarily agree completely. In the 1990s we will see more guidelines, and as a medical society and as staff organizations and specialty organizations, we will be dealing more with these types of issues.^{30, 31} Again, the distinction between rigid standards of care and more flexible practice guidelines becomes important.

References

- Standards of Medical Care for Patients with Diabetes Mellitus. *Diab Care* 1989;12:365-68.
- Robbins DC. A Bill of Rights. *Diab Care* 1989;12:371.
- Standards of Care. *Diab Forecast* 1989;55:66. (Sept).
- Setting the Standards. *Diab Spectrum* 1989;2:285-90 (Sept/Oct).
- Keiding NR, Root HF and Marble A. Importance of Control of Diabetes in Prevention of Vascular Complications. *JAMA* 1952;150:964-69.
- Jackson RL et al. Degenerative Changes in Young Diabetic Patients in Relationship to Level of Control. *Pediatrics* 1950;5:959-70.
- The Kroc Collaborative Study Group. Blood Glucose Control and the Evolution of Diabetic Retinopathy and Albuminuria. A Preliminary Multicenter Trial. *N Engl J Med* 1984;311:365-72.
- Holman RR et al. Prevention of Deterioration of Renal and Sensory-Nerve Function by more Intensive Management of Insulin-Dependent Diabetic Patients. *Lancet* 1983;1:204-08.
- Pirart J. Diabetes Mellitus and its Degenerative Complications: a Prospective Study of 4,400 Patients Observed Between 1947 and 1973. *Diab Care* 1978;1:168,252-63.
- Rosenstock J, Fribenc T and Raskin P. Effect of Glycemic Control on Microvascular Complications in Patients with Type I Diabetes Mellitus. *AM J Med* 1986;81:1012-18.
- University Group Diabetes Program. Effects of Hypoglycemic Agents on Vascular Complications in Patients with Adult-Onset Diabetes. III-Clinical Implications of UDGP Results. *JAMA* 1971;218:1400-10.
- The DCCT Research Group. Diabetes Control and Complications Trial (DCCT): Results of Feasibility Study. *Diab Care* 1978;1:101-19.
- Couet C et al. The Prevalence of Retinopathy is Similar in Diabetes Mellitus Secondary to Chronic Pancreatitis With or Without Pancreatectomy and Idiopathic Diabetes Mellitus. *Diab Care* 1985;8:323-28.
- Engerman R, Bloodworth JM, and Nelson S. Relationship of Microvascular Disease to Metabolic Control. *Diabetes* 1977;26:760-69.
- Mauer SM et al. Studies of Diabetic Nephropathy in Animals and Man. *Diabetes* 1976;25 (Suppl 2):850-57.
- Sox HC. Guidelines for Medical Practice: Necessary but not Sufficient. *J Gen Int Med* 1989;4:551-52.
- American College of Cardiology and American Heart Association Task Force. Guidelines for Coronary Angiography. *JACC* 1987;10:935-50.
- American College of Cardiology and American Heart Association Task Force. Guidelines for Percutaneous Transluminal Coronary Angioplasty. *JACC* 1988;12:529-45.
- American College of Cardiology and American Heart Association Task Force. Guidelines for Ambulatory Electrocardiography. *JACC* 1989;13:249-58.
- Leape LL. Unnecessary Surgery. *Health Services Research* 1989;24:351-407.
- The 1988 Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. *Arch Intern Med* 1988;148:1023-38.
- Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. *Arch Intern Med* 1988;148:36-69.
- McPhee SJ et al. Cost Containment Confronts Physicians. *Ann Intern Med* 1984;100:604-05.
- Obeler SK, LaForce FM. The Periodic Physical Examination in Asymptomatic Adults. *Ann Int Med* 1989;110:214-26.
- Muir A et al. General Practice Care of Non-Insulin-Dependent Diabetes with Fasting Blood Glucose Measurements. *Am J Med* 1982;73:637-40.
- Mogenson CE. Microalbuminuria Predicts Clinical Proteinuria and Early Mortality in Maturity-Onset Diabetes. *N Engl J Med* 1984;310:356-60.
- Rosenstock J, Raskin P. Early Diabetic Nephropathy: Assessment and Potential Therapeutic Interventions. *Diab Care* 1986;9:529-45.
- Keane WF et al. Angiotensin Converting Enzyme Inhibitors and Progressive Renal Insufficiency. *Ann Int Med* 1989;111:503-16.
- Cowie CC et al. Disparities in Incidence of Diabetic End-Stage Disease According to Race and Type of Diabetes. *N Engl J Med* 1989;321:1074-79.
- Brook RH. Practice Guidelines and Practicing Medicine - Are They Compatible? *JAMA* 1989;262:3027-30.
- Lomas J et al. Do Practice Guidelines Guide Practice? *N Engl J Med* 1989;321:1306-11.

A copy of "Standards of Medical Care for Patients with Diabetes Mellitus" appears in Diabetes Care 12:365-68, May 1989.

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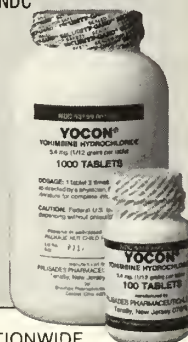
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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (September, 1940)

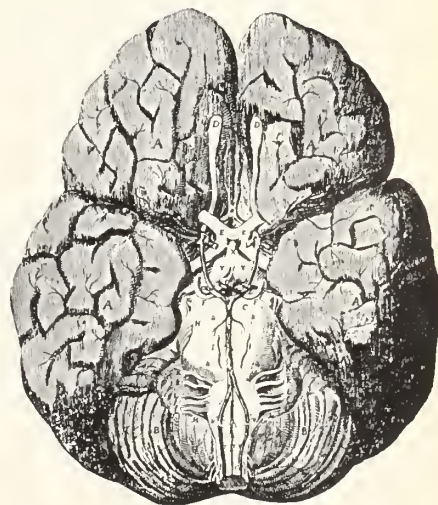
The lead article is entitled "The Circle of Willis: Its Angles and Its Aneurysms" and is written by Drs C.A. McDonald and M. Korb. After an initial description of the clinical and neuropathologic distinctions between spontaneous apopleptic hemorrhages of intracerebral and subarachnoid origins, the authors proceed to summarize Willis's description of the ventral arteries at the base of the human brain found in his 1664 treatise, *Cerebri Anatome*. The illustration of the so-called circle of Willis, found in this text (see figure below) is the work of the great English architect and artist, Christopher Wren. (*Ed. Note: Wren, who lived from 1632 to 1723, was variously an architect, mathematician and astronomer. He is best known for his design of St. Paul's Cathedral in London, built after the devastating London fire of 1666. He also designed some 52 other London churches many of which still stand today. The spires of a few of the churches on the east side of Providence, Rhode Island were patterned from Wren's texts on church architecture.*) The article by McDonald and Korb comments on the constituent arteries of this "circle" noting also that the configuration might more accurately be called a heptagon,

or better, a polygon. The article then provides the reader with the various hypotheses in the etiology of cerebral artery aneurysms, beginning with Eppinger's 1887 commentary attributing these dilatations to an innate weakness of the cerebral arteries at their points of junction and bifurcation.

The article offers the following conclusions: "The circle of Willis is not a circle. It is a polygon composed of straight arteries joining and branching at angles, where there is local weakness of the arterial wall. Developmental anomalies of the internal elastic layer predisposes to early arteriosclerosis and aneurysm formation at the angles. 49.5% of aneurysms were found on arteriosclerotic arteries. Developmental defect of the muscle of the media at the bifurcation angles predisposes to formation of so-called "congenital" aneurysms on arteries which are otherwise normal. 32.7% of aneurysms occurred on arteries which showed no pathologic changes other than the aneurysm. Gross anomaly of the circle of Willis itself is an important factor in the formation of cerebral aneurysms. The commonest gross defect of the circle of Willis is partial or complete absence of anastomosis between the basilar and the posterior communicating artery. The medical treatment of ruptured intracranial aneurysm is treatment of subarachnoid hem-

orrhage. The surgical treatment of repeated subarachnoid hemorrhages is the treatment of the ruptured aneurysm."

The second scientific contribution is authored by Dr R.L. Maynard and is entitled, "Reduction of Fractures of the Acetabulum with Penetration of the Head of the Femur into the Pelvis." The etiology of this pattern of fracture is ascribed to falls or blows, striking directly on the great trochanter and hip region. Symptoms and signs include a slight flexion, abduction and external rotation of the thigh with not more than one-half inch shortening of the involved extremity. There is limitation of motion of the hip with the feeling of resistance and par-



tial fixation, more than would be caused by pain and muscle spasm. The great trochanter is posterior to its normal location. The X-ray shows a fracture through the acetabulum with penetration of the head of the femur into the pelvis and fragments of the ischium pushed in before it.

The author describes three cases, a 53-year-old male who had fallen down stairs, a 53-year-old female who had slipped off a curbstone and had fallen full weight upon her right great trochanter, and a 53-year-old spastically paralytic male who had fallen on the sidewalk. Therapy, including prolonged longitudinal and lateral traction of the affected limb, resulted in gratifying recovery in all three cases.

The principal editorial, (*Ed. Note: published some 15 months prior to the Pearl Harbor attack and the entrance of the United States into World War II*), concerns medical preparedness and the efforts of the American Medical Association to determine the past and present status of every physician in the United States. The State Medical Society, through its Committee on Medical Preparedness (chaired by Dr Halsey DeWolf) has labored to encourage and hasten the return of this AMA questionnaire. The Committee shall assist the State government in the appointment of Medical Examiners when and if "... some form of Selective Service Bill passes the Congress."

Various Society Committee reports are published, including a somewhat discouraging summary by the Committee on Compulsory Membership in the State Society (of the approximately 1,000 doctors in Rhode Island as of 1940, "... a scant 486 are state society members.") The Committee on Education reports on the successful series of fifteen-minute weekly radio talks inaugu-

rated in December of 1938 which prompted 1,079 letters from the public requesting copies of the presentations.

Notice is published of Civil Service examinations to be held for medical officer positions in federal service, including the Veterans Administration, the Indian Service and the United States Public Health Service. Yearly salaries range from \$3,200 to \$4,600.

Obituaries are published following the deaths of Dr G.A. Blumer, the distinguished superintendent of Butler Hospital until 1922, and Dr J.E. Kerney, one of the leading urological surgeons of Rhode Island.

Twenty Five Years Ago (September, 1965)

The lead article is a report of a fatal case of *Listeria monocytogenes* meningoencephalitis in a newborn infant, and is written by Drs L. Falkenburg, E. West, V. Gideon and Mr. A. Troppoli. The report describes a 13-day-old white male infant hospitalized with a 24-hour history of fever and convulsions. A lumbar puncture produces a cloudy spinal fluid with numerous white blood cells, elevated protein content, depressed sugar concentration and gram positive cocci indicating meningitis. Despite vigorous treatment with a range of antibiotics, the infant died on the third hospital day. *Listeria monocytogenes* is recovered both from blood and spinal fluid. The bacteriologic diagnosis is confirmed by an outside laboratory. An autopsy examination reveals an acute, suppurative meningoencephalitis and an acute interstitial pneumonitis. The article describes the history of *Listeria* infection in humans noting that a gram positive diphtheroid pleomorphic rod was first noted in human meningitis in 1915. The pres-

ence of the organism in numerous vertebrate species suggests that wild animals form a natural reservoir for the occasional infection in humans. The organism as the basis for central nervous system infection has been reported in over 200 published cases from 25 different countries. The authors also describe the characteristic bacteriologic features of this small, motile rod.

The second scientific contribution is an intriguing inquiry by Dr M. Duke concerning the possibly salutary place of phlebotomy as a therapy for angina pectoris. The article briefly summarizes the role of phlebotomy (ie, blood letting, cupping or venesection) during the last two centuries. A number of medical observers in the nineteenth century noted that the typical patient with angina pectoris is a "plethoric obese patient" and "... blood letting was used as a nonspecific and empiric remedy" to lessen the plethoric state of the blood in such individuals. The author concludes: "Whether changes in hematocrit, blood viscosity, blood volume, or circulatory dynamics prove to be significant factors in the symptoms caused by this disease, whether indeed some of these changes are present at all, whether they are coincidental findings in this disease rather than of etiologic significance, or whether the patient with coronary artery disease can indeed be benefitted by phlebotomy, is far from clear."

Drs L. Leone and M. Albala provide a progress report on the complexities of myeloma and the remissive capabilities of newer alkylating agents. The authors note first that the disease may have both a neoplastic component involving discrete or disseminated plasma cell proliferation, and a non-neoplastic component with such manifestations as primary amyloidosis, macroglobu-

linemia and cryoglobulinemia. The paper than offers a clear biochemical and biophysical description of the macroglobulinemic proteins. Finally, the paper describes the uses and limitations of such agents as cyclophosphamide and L-phenylalanine mustard.

The lead editorial describes the amended Social Security Law (Public Law 89-97, 89th Congress, July 30, 1965), the so-called Medicare laws. The *Journal* prints the text of the new laws, particularly Title 1, and provides the reader with the legislative definitions of such terms as "extended care services," "post-hospital extended care services," "Christian Science extended care facility," and "reasonable cost." Exclusions from coverage are also listed. A briefer editorial also notes that self-employed physicians are now included in the Social Security Laws — on a compulsory basis.

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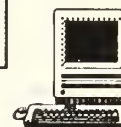
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Table 1.
Birth to 18 Months
Schedule: 2, 4, 6, 15, 18 Months*

Leading Causes of Death:
 Conditions originating in
 perinatal period
 Congenital anomalies
 Heart disease
 Injuries (nonmotor vehicle)
 Pneumonia/influenza

High-Risk Categories

Table 1. Birth to 18 Months

HR1 Infants with a family history of childhood hearing impairment or a personal history of congenital perinatal infection with herpes, syphilis, rubella, cytomegalovirus, or toxoplasmosis, malformations involving the head or neck (e.g., dysmorphic and syndromal abnormalities, cleft palate, abnormal pinna), birthweight below 1500 g, bacterial meningitis, hyperbilirubinemia requiring exchange transfusion, or severe perinatal asphyxia (Apgar scores of 0–3, absence of spontaneous respirations for 10 minutes, or hypotonia at 2 hours of age)

HR2 Infants who live in or frequently visit housing built before 1950 that is dilapidated or undergoing renovation; who come in contact with other children with known lead toxicity, who live near lead processing plants or whose parents or household members work in a lead-related occupation, or who live near busy highways or hazardous waste sites

HR3 Infants living in areas with inadequate water fluoridation (less than 0.7 parts per million)

HR4 Newborns of Caribbean, Latin American, Asian, Mediterranean, or African descent

SCREENING

Height and weight
 Hemoglobin and hematocrit¹
HIGH-RISK GROUPS
 Hearing² (HR1)
 Erythrocyte protoporphyrin
 (HR2)

This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:

- Developmental disorders
- Musculoskeletal malformations
- Cardiac anomalies
- Genitourinary disorders
- Metabolic disorders
- Speech problems
- Behavioral disorders
- Parent/family dysfunction

PARENT COUNSELING

Diet
 Breastfeeding
 Nutrient intake, especially iron-rich foods

Injury Prevention
 Child safety seats
 Smoke detector
 Hot water heater temperature
 Stairway gates, window guards, pool fence
 Storage of drugs and toxic chemicals
 Syrup of ipecac, poison control telephone number

Dental Health
 Baby bottle tooth decay

Other Primary Preventive Measures
 Effects of passive smoking

IMMUNIZATIONS & CHEMOPROPHYLAXIS

Diphtheria-tetanus-pertussis (DTP) vaccine³
 Oral poliovirus vaccine (OPV)⁴
 Measles-mumps-rubella (MMR) vaccine⁵
Haemophilus influenzae type b (Hib) conjugate vaccine⁶
HIGH-RISK GROUPS
 Fluoride supplements (HR3)

FIRST WEEK

Ophthalmic antibiotics⁷
 Hemoglobin electrophoresis (HR4)⁷
 T4/TSH⁸
 Phenylalanine⁸
 Hearing (HR1)

Remain Alert For:
 Ocular misalignment
 Tooth decay
 Signs of child abuse or neglect

*Five visits are required for immunizations. Because of lack of data and differing patient risk profiles, the scheduling of additional visits and the frequency of the individual preventive services listed in this table are left to clinical discretion (except as indicated in other footnotes).

1. Once during infancy. 2. At age 18-month visit, if not tested earlier. 3. At ages 2, 4, 6, and 15 months. 4. At ages 2, 4, and 15 months. 5. At age 15 months. 6. At age 18 months. 7. At birth. 8. Days 3 to 6 preferred for testing.

Table 2.
Ages 2-6
Schedule: See Footnote*

Leading Causes of Death:
Injuries (nonmotor vehicle)
Motor vehicle crashes
Congenital anomalies
Homicide
Heart disease

High-Risk Categories

Table 2. Ages 2-6

SCREENING	PATIENT & PARENT COUNSELING	IMMUNIZATIONS & CHEMOPROPHYLAXIS
<p>Height and weight Blood pressure Eye exam for amblyopia and strabismus¹ Urinalysis for bacteriuria</p> <p><i>HIGH-RISK GROUPS</i></p> <p>Erythrocyte protoporphyrin² (HR1) Tuberculin skin test (PPD) (HR2) Hearing³ (HR3)</p>	<p>Diet and Exercise Sweets and between-meal snacks, iron-enriched foods, sodium Caloric balance Selection of exercise program</p> <p>Injury Prevention Safety belts Smoke detector Hot water heater temperature Window guards and pool fence Bicycle safety helmets Storage of drugs, toxic chemicals, matches, and firearms Syrup of ipecac, poison control telephone number</p> <p>Dental Health Tooth brushing and dental visits</p>	<p>Diphtheria-tetanus-pertussis (DTP) vaccine⁴ Oral poliovirus vaccine (OPV)⁴</p> <p><i>HIGH-RISK GROUPS</i></p> <p>Fluoride supplements (HR5)</p>
<p>This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:</p> <ul style="list-style-type: none"> Developmental disorders Speech problems Behavioral and learning disorders Parent/family dysfunction 	<p>Other Primary Preventive Measures Effects of passive smoking</p> <p><i>HIGH-RISK GROUPS</i></p> <p>Skin protection from ultraviolet light (HR4)</p>	<p>Remain Alert For: Vision disorders Dental decay, malalignment, premature loss of teeth, mouth breathing Signs of child abuse or neglect Abnormal bereavement</p>

*One visit is required for immunizations. Because of lack of data and differing patient risk profiles, the scheduling of additional visits and the frequency of the individual preventive services listed in this table are left to clinical discretion (except as indicated in other footnotes).

1. Ages 3-4. 2. Annually. 3. Before age 3, if not tested earlier. 4. Once between ages 4 and 6.

HR1 Children who live in or frequently visit housing built before 1950 that is dilapidated or undergoing renovation, who come in contact with other children with known lead toxicity, who live near lead processing plants or whose parents or household members work in a lead-related occupation, or who live near busy highways or hazardous waste sites

HR2 Household members of persons with tuberculosis or others at risk for close contact with the disease, recent immigrants or refugees from countries in which tuberculosis is common (e.g., Asia, Africa, Central and South America, Pacific Islands), family members of migrant workers, residents of homeless shelters, or persons with certain underlying medical disorders

HR3 Children with a family history of childhood hearing impairment or a personal history of congenital perinatal infection with herpes, syphilis, rubella, cytomegalovirus, or toxoplasmosis, malformations involving the head or neck (e.g., dysmorphic and syndromal abnormalities, cleft palate, abnormal pinna), birthweight below 1500 g, bacterial meningitis, hyperbilirubinemia requiring exchange transfusion, or severe perinatal asphyxia (Apgar scores of 0-3, absence of spontaneous respirations for 10 minutes, or hypotonia at 2 hours of age)

HR4 Children with increased exposure to sunlight

HR5 Children living in areas with inadequate water fluoridation (less than 0.7 parts per million)

Table 3.
Ages 7-12
 Schedule: See Footnote*

Leading Causes of Death:
 Motor vehicle crashes
 Injuries (nonmotor vehicle)
 Congenital anomalies
 Leukemia
 Homicide
 Heart disease

High-Risk Categories

Table 3. Ages 7-12

HR1 Household members of persons with tuberculosis or others at risk for close contact with the disease, recent immigrants or refugees from countries in which tuberculosis is common (e.g., Asia, Africa, Central and South America, Pacific Islands), family members of migrant workers; residents of homeless shelters; or persons with certain underlying medical disorders
HR2 Children with increased exposure to sunlight
HR3 Children living in areas with inadequate water fluoridation (less than 0.7 parts per million)

SCREENING	PATIENT & PARENT COUNSELING	CHEMOPROPHYLAXIS
Height and weight Blood pressure <i>HIGH RISK GROUPS</i> Tuberculin skin test (PPD) (HR1)	Diet and Exercise Fat (especially saturated fat), cholesterol, sweets and between-meal snacks, sodium Caloric balance Selection of exercise program Injury Prevention Safety belts Smoke detector Storage of firearms, drugs, toxic chemicals, matches Bicycle safety helmets Dental Health Regular tooth brushing and dental visits Other Primary Preventive Measures <i>HIGH-RISK GROUPS</i> Skin protection from ultraviolet light (HR2)	<i>HIGH-RISK GROUPS</i> Fluoride supplements (HR3)
<p>This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:</p> <ul style="list-style-type: none"> Developmental disorders Scoliosis Behavioral and learning disorders Parent/family dysfunction 		
		<p>Remain Alert For: Vision disorders Diminished hearing Dental decay, malalignment, mouth breathing Signs of child abuse or neglect Abnormal bereavement</p>

*Because of lack of data and differing patient risk profiles, the scheduling of visits and the frequency of the individual preventive services listed in this table are left to clinical discretion.

Table 4.
Ages 13–18
Schedule: See Footnote*

Leading Causes of Death:
Motor vehicle crashes
Homicide
Suicide
Injuries (nonmotor vehicle)
Heart disease

High-Risk Categories

Table 4. Ages 13–18

SCREENING

History

Dietary intake
Physical activity
Tobacco/alcohol/drug use
Sexual practices

Physical Exam

Height and weight
Blood pressure

HIGH-RISK GROUPS

Complete skin exam (HR1)
Clinical testicular exam (HR2)

Laboratory/Diagnostic Procedures

HIGH-RISK GROUPS

Rubella antibodies (HR3)
VDRL/RPR (HR4)
Chlamydial testing (HR5)
Gonorrhea culture (HR6)
Counseling and testing for HIV (HR7)
Tuberculin skin test (PPD) (HR8)
Hearing (HR9)
Papanicolaou smear (HR10)¹

COUNSELING

Diet and Exercise

Fat (especially saturated fat), cholesterol, sodium, iron,² calcium²
Caloric balance
Selection of exercise program

Substance Use

Tobacco: cessation/primary prevention

Alcohol and other drugs: cessation/primary prevention

Driving/other dangerous activities while under the influence

Treatment for abuse

HIGH-RISK GROUPS

Sharing/using unsterilized needles and syringes (HR12)

Sexual Practices

Sexual development and behavior³

Sexually transmitted diseases: partner selection, condoms

Unintended pregnancy and contraceptive options

Injury Prevention

Safety belts

Safety helmets

Violent behavior⁴

Firearms⁴

Smoke detector

Dental Health

Regular tooth brushing, flossing, dental visits

Other Primary

Preventive Measures

HIGH-RISK GROUPS

Discussion of hemoglobin testing (HR13)

Skin protection from ultraviolet light (HR14)

IMMUNIZATIONS & CHEMOPROPHYLAXIS

Tetanus-diphtheria (Td) booster⁵

HIGH-RISK GROUPS

Fluoride supplements (HR15)

This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:

Developmental disorders
Scoliosis
Behavioral and learning disorders
Parent/family dysfunction

Remain Alert For:

Depressive symptoms
Suicide risk factors (HR11)
Abnormal bereavement
Tooth decay, malalignment, gingivitis
Signs of child abuse and neglect.

*One visit is required for immunizations. Because of lack of data and differing patient risk profiles, the scheduling of additional visits and the frequency of the individual preventive services listed in this table are left to clinical discretion (except as indicated in other footnotes).

1. Every 1–3 years. 2. For females. 3. Often best performed early in adolescence and with the involvement of parents. 4. Especially for males. 5. Once between ages 14 and 16.

HR1 Persons with increased recreational or occupational exposure to sunlight, a family or personal history of skin cancer, or clinical evidence of precursor lesions (e.g., dysplastic nevi, certain congenital nevi)

HR2 Males with a history of cryptorchidism, orchiopexy, or testicular atrophy

HR3 Females of childbearing age lacking evidence of immunity

HR4 Persons who engage in sex with multiple partners in areas in which syphilis is prevalent, prostitutes, or contacts of persons with active syphilis

HR5 Persons who attend clinics for sexually transmitted diseases, attend other high-risk health care facilities (e.g., adolescent and family planning clinics), or have other risk factors for chlamydial infection (e.g., multiple sexual partners or a sexual partner with multiple sexual contacts)

HR6 Persons with multiple sexual partners or a sexual partner with multiple contacts, sexual contacts of persons with culture-proven gonorrhea, or persons with a history of repeated episodes of gonorrhea

HR7 Persons seeking treatment for sexually transmitted diseases, homosexual and bisexual men, past or present intravenous (IV) drug users, persons with a history of prostitution or multiple sexual partners, women whose past or present sexual partners were HIV-infected, bisexual, or IV drug users, persons with long-term residence or birth in an area with high prevalence of HIV infection, or persons with a history of transfusion between 1978 and 1985

HR8 Household members of persons with tuberculosis or others at risk for close contact with the disease, recent immigrants or refugees from countries in which tuberculosis is common (e.g., Asia, Africa, Central and South America, Pacific Islands); migrant workers, residents of correctional institutions or homeless shelters, or persons with certain underlying medical disorders

HR9 Persons exposed regularly to excessive noise in recreational or other settings

HR10 Females who are sexually active or (if the sexual history is thought to be unreliable) aged 18 or older

HR11 Recent divorce, separation, unemployment, depression, alcohol or other drug abuse, serious medical illnesses, living alone, or recent bereavement

HR12 Intravenous drug users

HR13 Persons of Caribbean, Latin American, Asian, Mediterranean, or African descent

HR14 Persons with increased exposure to sunlight

HR15 Persons living in areas with inadequate water fluoridation (less than 0.7 parts per million)

Table 5.
Ages 19–39
Schedule: Every 1–3 Years*

Leading Causes of Death:
Motor vehicle crashes
Homicide
Suicide
Injuries (nonmotor vehicle)
Heart disease

High-Risk Categories

SCREENING	COUNSELING	IMMUNIZATIONS
<p>History Dietary intake Physical activity Tobacco/alcohol/drug use Sexual practices</p> <p>Physical Exam Height and weight Blood pressure</p> <p>HIGH-RISK GROUPS Complete oral cavity exam (HR1) Palpation for thyroid nodules (HR2) Clinical breast exam (HR3) Clinical testicular exam (HR4) Complete skin exam (HR5)</p> <p>Laboratory/Diagnostic Procedures Nonfasting total blood cholesterol Papanicolaou smear¹</p> <p>HIGH-RISK GROUPS Fasting plasma glucose (HR6) Rubella antibodies (HR7) VDRL/RPR (HR8) Urinalysis for bacteriuria (HR9) Chlamydial testing (HR10) Gonorrhea culture (HR11) Counseling and testing for HIV (HR12) Hearing (HR13) Tuberculin skin test (PPD) (HR14) Electrocardiogram (HR15) Mammogram (HR3) Colonoscopy (HR16)</p>	<p>Diet and Exercise Fat (especially saturated fat), cholesterol, complex carbohydrates, fiber, sodium, iron², calcium² Caloric balance Selection of exercise program</p> <p>Substance Use Tobacco: cessation/primary prevention Alcohol and other drugs: Limiting alcohol consumption Driving/other dangerous activities while under the influence Treatment for abuse</p> <p>HIGH-RISK GROUPS Sharing/using unsterilized needles and syringes (HR18)</p> <p>Sexual Practices Sexually transmitted diseases: partner selection, condoms, anal intercourse Unintended pregnancy and contraceptive options</p> <p>Injury Prevention Safety belts Safety helmets Violent behavior³ Firearms³ Smoke detector Smoking near bedding or upholstery</p> <p>HIGH-RISK GROUPS Back-conditioning exercises (HR19) Prevention of childhood injuries (HR20) Falls in the elderly (HR21)</p> <p>Dental Health Regular tooth brushing, flossing, dental visits</p> <p>Other Primary Preventive Measures</p> <p>HIGH-RISK GROUPS Discussion of hemoglobin testing (HR22) Skin protection from ultraviolet light (HR23)</p>	<p>Tetanus-diphtheria (Td) booster⁴</p> <p>HIGH-RISK GROUPS Hepatitis B vaccine (HR24) Pneumococcal vaccine (HR25) Influenza vaccine⁵ (HR26) Measles-mumps-rubella vaccine (HR27)</p> <p>This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:</p> <p>Chronic obstructive pulmonary disease Hepatobiliary disease Bladder cancer Endometrial disease Travel-related illness Prescription drug abuse Occupational illness and injuries</p> <p>Remain Alert For: Depressive symptoms Suicide risk factors (HR17) Abnormal bereavement Malignant skin lesions Tooth decay, gingivitis Signs of physical abuse</p>

Table 5. Ages 19–39

- HR1** Persons with exposure to tobacco or excessive amounts of alcohol, or those with suspicious symptoms or lesions detected through self-examination.
- HR2** Persons with a history of upper-body irradiation.
- HR3** Women aged 35 and older with a family history of premenopausally diagnosed breast cancer in a first-degree relative.
- HR4** Men with a history of cryptorchidism, orchiopexy, or testicular atrophy.
- HR5** Persons with family or personal history of skin cancer, increased occupational or recreational exposure to sunlight, or clinical evidence of precursor lesions (e.g., dysplastic nevi, certain congenital nevi).
- HR6** The markedly obese, persons with a family history of diabetes, or women with a history of gestational diabetes.
- HR7** Women lacking evidence of immunity.
- HR8** Prostitutes, persons who engage in sex with multiple partners in areas in which syphilis is prevalent, or contacts of persons with active syphilis.
- HR9** Persons with diabetes.
- HR10** Persons who attend clinics for sexually transmitted diseases, attend other high-risk health care facilities (e.g., adolescent and family planning clinics), or have other risk factors for chlamydial infection (e.g., multiple sexual partners or a sexual partner with multiple sexual contacts, age less than 20).
- HR11** Prostitutes, persons with multiple sexual partners or a sexual partner with multiple contacts, sexual contacts of persons with culture-proven gonorrhea, or persons with a history of repeated episodes of gonorrhea.
- HR12** Persons seeking treatment for sexually transmitted diseases, homosexual and bisexual men, past or present intravenous (IV) drug users, persons with a history of prostitution or multiple sexual partners, women whose past or present sexual partners were HIV-infected, bisexual, or IV drug users, persons with long-term residence or birth in an area with high prevalence of HIV infection, or persons with a history of transfusion between 1978 and 1985.
- HR13** Persons exposed regularly to excessive noise.
- HR14** Household members of persons with tuberculosis or others at risk for close contact with the disease (e.g., staff of tuberculosis clinics, shelters for the homeless, nursing homes, substance abuse treatment facilities, dialysis units, correctional institutions); recent immigrants or refugees from countries in which tuberculosis is common, migrant workers, residents of nursing homes, correctional institutions, or homeless shelters; or persons with certain underlying medical disorders (e.g., HIV infection).
- HR15** Men who would endanger public safety were they to experience sudden cardiac events (e.g., commercial airline pilots).
- HR16** Persons with a family history of familial polyposis coli or cancer family syndrome.
- HR17** Recent divorce, separation, unemployment, depression, alcohol or other drug abuse, serious medical illnesses, living alone, or recent bereavement.
- HR18** Intravenous drug users.
- HR19** Persons at increased risk for low back injury because of past history, body configuration, or type of activities.
- HR20** Persons with children in the home or automobile.
- HR21** Persons with older adults in the home.
- HR22** Young adults of Caribbean, Latin American, Asian, Mediterranean, or African descent.
- HR23** Persons with increased exposure to sunlight.
- HR24** Homosexually active men, intravenous drug users, recipients of some blood products, or persons in health-related jobs with frequent exposure to blood or blood products.
- HR25** Persons with medical conditions that increase the risk of pneumococcal infection (e.g., chronic cardiac or pulmonary disease, sickle cell disease, nephrotic syndrome, Hodgkin's disease, asplenia, diabetes mellitus, alcoholism, cirrhosis, multiple myeloma, renal disease, or conditions associated with immunosuppression).
- HR26** Residents of chronic care facilities or persons suffering from chronic cardiopulmonary disorders, metabolic diseases (including diabetes mellitus), hemoglobinopathies, immunosuppression, or renal dysfunction.
- HR27** Persons born after 1956 who lack evidence of immunity to measles (receipt of live vaccine on or after first birthday, laboratory evidence of immunity, or a history of physician-diagnosed measles).

*The recommended schedule applies only to the periodic visit itself. The frequency of the individual preventive services listed in this table is left to clinical discretion, except as indicated in other footnotes.

1. Every 1–3 years. 2. For women. 3. Especially for young males. 4. Every 10 years. 5. Annually.

Table 6.
Ages 40–64
Schedule: Every 1–3 Years*

Leading Causes of Death:
Heart disease
Lung cancer
Cerebrovascular disease
Breast cancer
Colorectal cancer
Obstructive lung disease

SCREENING	COUNSELING	IMMUNIZATIONS
History Dietary intake Physical activity Tobacco/alcohol/drug use Sexual practices Physical Exam Height and weight Blood pressure Clinical breast exam ¹ HIGH-RISK GROUPS Complete skin exam (HR1) Complete oral cavity exam (HR2) Palpation for thyroid nodules (HR3) Auscultation for carotid bruits (HR4) Laboratory/Diagnostic Procedures Nonfasting total blood cholesterol Papanicolaou smear ² Mammogram ³ HIGH-RISK GROUPS Fasting plasma glucose (HR5) VDRL/RPR (HR6) Urinalysis for bacteriuria (HR7) Chlamydial testing (HR8) Gonorrhea culture (HR9) Counseling and testing for HIV (HR10) Tuberculin skin test (PPD) (HR11) Hearing (HR12) Electrocardiogram (HR13) Fecal occult blood/sigmoidoscopy (HR14) Fecal occult blood/colonoscopy (HR15) Bone mineral content (HR16)	Diet and Exercise Fat (especially saturated fat), cholesterol, complex carbohydrates, fiber, sodium, calcium ⁴ Caloric balance Selection of exercise program Substance Use Tobacco cessation Alcohol and other drugs: Limiting alcohol consumption Driving/other dangerous activities while under the influence Treatment for abuse HIGH-RISK GROUPS Sharing/using unsterilized needles and syringes (HR19) Sexual Practices Sexually transmitted diseases; partner selection, condoms, anal intercourse Unintended pregnancy and contraceptive options Injury Prevention Safety belts Safety helmets Smoke detector Smoking near bedding or upholstery HIGH-RISK GROUPS Back-conditioning exercises (HR20) Prevention of childhood injuries (HR21) Falls in the elderly (HR22) Dental Health Regular tooth brushing, flossing, and dental visits Other Primary Preventive Measures HIGH-RISK GROUPS Skin protection from ultraviolet light (HR23) Discussion of aspirin therapy (HR24) Discussion of estrogen replacement therapy (HR25)	Tetanus-diphtheria (Td) booster⁵ HIGH-RISK GROUPS Hepatitis B vaccine (HR26) Pneumococcal vaccine (HR27) Influenza vaccine (HR28) ⁶ <p>This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:</p> <p>Chronic obstructive pulmonary disease Hepatobiliary disease Bladder cancer Endometrial disease Travel-related illness Prescription drug abuse Occupational illness and injuries</p> <p>Remain Alert For: Depressive symptoms Suicide risk factors (HR17) Abnormal bereavement Signs of physical abuse or neglect Malignant skin lesions Peripheral arterial disease (HR18) Tooth decay, gingivitis, loose teeth</p>
<p>*The recommended schedule applies only to the periodic visit itself. The frequency of the individual preventive services listed in this table is left to clinical discretion, except as indicated in other footnotes.</p>		

1. Annually for women. 2. Every 1–3 years for women. 3. Every 1–2 years for women beginning at age 50 (age 35 for those at increased risk). 4. For women. 5. Every 10 years. 6. Annually.

Table 6. Ages 40–64

HR1 Persons with a family or personal history of skin cancer, increased occupational or recreational exposure to sunlight, or clinical evidence of precursor lesions (e.g., dysplastic nevi, certain congenital nevi)

HR2 Persons with exposure to tobacco or excessive amounts of alcohol, or those with suspicious symptoms or lesions detected through self-examination

HR3 Persons with a history of upper-body irradiation

HR4 Persons with risk factors for cerebrovascular or cardiovascular disease (e.g., hypertension, smoking, CAD, atrial fibrillation, diabetes) or those with neurologic symptoms (e.g., transient ischemic attacks) or a history of cerebrovascular disease

HR5 The markedly obese, persons with a family history of diabetes, or women with a history of gestational diabetes

HR6 Prostitutes, persons who engage in sex with multiple partners in areas in which syphilis is prevalent, or contacts of persons with active syphilis

HR7 Persons with diabetes

HR8 Persons who attend clinics for sexually transmitted diseases, attend other high-risk health care facilities (e.g., adolescent and family planning clinics), or have other risk factors for chlamydial infection (e.g., multiple sexual partners or a sexual partner with multiple sexual contacts)

HR9 Prostitutes, persons with multiple sexual partners or a sexual partner with multiple contacts, sexual contacts of persons with culture-proven gonorrhea, or persons with a history of repeated episodes of gonorrhea

HR10 Persons seeking treatment for sexually transmitted diseases, homosexual and bisexual men, past or present intravenous (IV) drug users, persons with a history of prostitution or multiple sexual partners, women whose past or present sexual partners were HIV-infected, bisexual, or IV drug users, persons with long-term residence or birth in an area with high prevalence of HIV infection, or persons with a history of transfusion between 1978 and 1985

HR11 Household members of persons with tuberculosis or others at risk for close contact with the disease (e.g., staff of tuberculosis clinics, shelters for the homeless, nursing homes, substance abuse treatment facilities, dialysis units, correctional institutions), recent immigrants or refugees from countries in which tuberculosis is common (e.g., Asia, Africa, Central and South America, Pacific Islands), migrant workers, residents of nursing homes, correctional institutions, or homeless shelters, or persons with certain underlying medical disorders (e.g., HIV infection)

HR12 Persons exposed regularly to excessive noise

HR13 Men with two or more cardiac risk factors (high blood cholesterol, hypertension, cigarette smoking, diabetes mellitus, family history of CAD), men who would endanger public safety were they to experience sudden cardiac events (e.g., commercial airline pilots), or sedentary or high-risk males planning to begin a vigorous exercise program

HR14 Persons aged 50 and older who have first-degree relatives with colorectal cancer, a personal history of endometrial, ovarian, or breast cancer, or a previous diagnosis of inflammatory bowel disease, adenomatous polyps, or colorectal cancer

HR15 Persons with a family history of familial polyposis coli or cancer family syndrome

HR16 Perimenopausal women at increased risk for osteoporosis (e.g., Caucasian race, bilateral oophorectomy before menopause, slender build) and for whom estrogen replacement therapy would otherwise not be recommended

HR17 Recent divorce, separation, unemployment, depression, alcohol or other drug abuse, serious medical illnesses, living alone, or recent bereavement

HR18 Persons over age 50, smokers, or persons with diabetes mellitus

HR19 Intravenous drug users

HR20 Persons at increased risk for low back injury because of past history, body configuration, or type of activities

HR21 Persons with children in the home or automobile

HR22 Persons with older adults in the home

HR23 Persons with increased exposure to sunlight

HR24 Men who have risk factors for myocardial infarction (e.g., high blood cholesterol, smoking, diabetes mellitus, family history of early-onset CAD) and who lack a history of gastrointestinal or other bleeding problems, and other risk factors for bleeding or cerebral hemorrhage

HR25 Perimenopausal women at increased risk for osteoporosis (e.g., Caucasian, low bone mineral content, bilateral oophorectomy before menopause or early menopause, slender build) and who are without known contraindications (e.g., history of undiagnosed vaginal bleeding, active liver disease, thromboembolic disorders, hormone-dependent cancer)

HR26 Homosexually active men, intravenous drug users, recipients of some blood products, or persons in health-related jobs with frequent exposure to blood or blood products

HR27 Persons with medical conditions that increase the risk of pneumococcal infection (e.g., chronic cardiac or pulmonary disease, sickle cell disease, nephrotic syndrome, Hodgkin's disease, asplenia, diabetes mellitus, alcoholism, cirrhosis, multiple myeloma, renal disease or conditions associated with immunosuppression)

HR28 Residents of chronic care facilities and persons suffering from chronic cardiopulmonary disorders, metabolic diseases (including diabetes

Table 7.
Ages 65 and Over
Schedule: Every Year*

Leading Causes of Death:
Heart disease
Cerebrovascular disease
Obstructive lung disease
Pneumonia/influenza
Lung cancer
Colorectal cancer

High-Risk Categories

Table 7. Ages 65 and Over

SCREENING

History

Prior symptoms of transient ischemic attack
Dietary intake
Physical activity
Tobacco/alcohol/drug use
Functional status at home

Physical Exam

Height and weight
Blood pressure
Visual acuity
Hearing and hearing aids
Clinical breast exam¹

HIGH-RISK GROUPS

Auscultation for carotid bruits (HR1)
Complete skin exam (HR2)
Complete oral cavity exam (HR3)
Palpation of thyroid nodules (HR4)

Laboratory/Diagnostic Procedures

Nonfasting total blood cholesterol
Dipstick urinalysis
Mammogram²
Thyroid function tests³

HIGH-RISK GROUPS

Fasting plasma glucose (HR5)
Tuberculin skin test (PPD) (HR6)
Electrocardiogram (HR7)
Papanicolaou smear⁴ (HR8)
Fecal occult blood/Sigmoidoscopy (HR9)
Fecal occult blood/Colonoscopy (HR10)

COUNSELING

Diet and Exercise

Fat (especially saturated fat), cholesterol, complex carbohydrates, fiber, sodium, calcium³
Caloric balance
Selection of exercise program

Substance Use

Tobacco cessation
Alcohol and other drugs:
Limiting alcohol consumption
Driving/other dangerous activities while under the influence
Treatment for abuse

Injury Prevention

Prevention of falls
Safety belts
Smoke detector
Smoking near bedding or upholstery
Hot water heater temperature
Safety helmets

HIGH-RISK GROUPS

Prevention of childhood injuries (HR12)

Dental Health

Regular dental visits, tooth brushing, flossing

Other Primary

Preventive Measures

Glaucoma testing by eye specialist

HIGH-RISK GROUPS

Discussion of estrogen replacement therapy (HR13)
Discussion of aspirin therapy (HR14)
Skin protection from ultraviolet light (HR15)

IMMUNIZATIONS

Tetanus-diphtheria (Td) booster⁵

Influenza vaccine¹

Pneumococcal vaccine

HIGH-RISK GROUPS

Hepatitis B vaccine (HR16)

This list of preventive services is not exhaustive.

It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include:

Chronic obstructive pulmonary disease
Hepatobiliary disease
Bladder cancer
Endometrial disease
Travel-related illness
Prescription drug abuse
Occupational illness and injuries

Remain Alert For:

Depression symptoms
Suicide risk factors (HR11)
Abnormal bereavement
Changes in cognitive function
Medications that increase risk of falls
Signs of physical abuse or neglect
Malignant skin lesions
Peripheral arterial disease
Tooth decay, gingivitis, loose teeth

*The recommended schedule applies only to the periodic visit itself. The frequency of the individual preventive services listed in this table is left to clinical discretion, except as indicated in other footnotes.

1. Annually. 2. Every 1-2 years for women until age 75, unless pathology detected. 3. For women. 4. Every 1-3 years. 5. Every 10 years.

Table 8.
Pregnant Women¹

FIRST PRENATAL VISIT		
SCREENING History Genetic and obstetric history Dietary intake Tobacco/alcohol/drug use Risk factors for intrauterine growth retardation and low birthweight Prior genital herpetic lesions Laboratory/Diagnostic Procedures Blood pressure Hemoglobin and hematocrit ABO/Rh typing Rh(D) and other antibody screen VDRL/RPR Hepatitis B surface antigen (HBsAg) Urinalysis for bacteriuria Gonorrhea culture <i>HIGH-RISK GROUPS</i> Hemoglobin electrophoresis (HR1) Rubella antibodies (HR2) Chlamydial testing (HR3) Counseling and testing for HIV (HR4)	COUNSELING Nutrition Tobacco use Alcohol and other drug use Safety belts <i>HIGH-RISK GROUPS</i> Discuss amniocentesis (HR5) Discuss risks of HIV infection (HR4)	This list of preventive services is not exhaustive. It reflects only those topics reviewed by the U.S. Preventive Services Task Force. Clinicians may wish to add other preventive services on a routine basis, and after considering the patient's medical history and other individual circumstances. Examples of target conditions not specifically examined by the Task Force include: Counseling on warning signs and symptoms Physical findings of abdominal and cervical examination Tay-Sachs disease Childbirth education Teratogenic and fetotoxic exposures
	Remain Alert For: Signs of physical abuse	
FOLLOW-UP VISITS Schedule: See Footnote*		
1. See also Tables 4–6 for other preventive services for women. 2. Women with access to counseling and follow-up services, skilled high-resolution ultrasound and amniocentesis capabilities, and reliable, standardized laboratories.	SCREENING Blood pressure Urinalysis for bacteriuria Screening Tests at Specific Gestational Ages 14–16 Weeks: Maternal serum alpha-fetoprotein (MSAFP) ² Ultrasound cephalometry (HR8) 24–28 Weeks: 50 g oral glucose tolerance test Rh(D) antibody (HR9) Gonorrhea culture (HR10) VDRL/RPR (HR11) Hepatitis B surface antigen (HBsAg) (HR12) Counseling and testing for HIV (HR13) 36 Weeks: Ultrasound exam (HR14)	COUNSELING Nutrition Safety belts Discuss meaning of upcoming tests <i>HIGH-RISK GROUPS</i> Tobacco use (HR6) Alcohol and other drug use (HR7)
		Remain Alert For: Signs of physical abuse
*Because of lack of data and differing patient risk profiles, the scheduling of visits and the frequency of the individual preventive services listed in this table are left to clinical discretion, except for those indicated at specific gestational ages.		

Table 8. Pregnant Women

- HR1 Black women
 HR2 Women lacking evidence of immunity (proof of vaccination after the first birthday or laboratory evidence of immunity)
 HR3 Women who attend clinics for sexually transmitted diseases, attend other high-risk health care facilities (e.g., adolescent and family planning clinics), or have other risk factors for chlamydial infection (e.g., multiple sexual partners or a sexual partner with multiple sexual contacts)
 HR4 Women seeking treatment for sexually transmitted diseases, past or present intravenous (IV) drug users, women with a history of prostitution or multiple sexual partners, women whose past or present sexual partners were HIV-infected, bisexual, or IV drug users, women with long-term residence or birth in an area with high prevalence of HIV infection in women, or women with a history of transfusion between 1978 and 1985
 HR5 Women aged 35 and older
 HR6 Women who continue to smoke during pregnancy
 HR7 Women with excessive alcohol consumption during pregnancy
 HR8 Women with uncertain menstrual histories or risk factors for intrauterine growth retardation (e.g., hypertension, renal disease, short maternal stature, low prepregnancy weight, failure to gain weight during pregnancy, smoking, alcohol and other drug abuse, and history of a previous fetal death or growth-retarded baby)
 HR9 Unsensitized Rh-negative women
 HR10 Women with multiple sexual partners or a sexual partner with multiple contacts, or sexual contacts of persons with culture-proven gonorrhea
 HR11 Women who engage in sex with multiple partners in areas in which syphilis is prevalent, or contacts of persons with active syphilis
 HR12 Women who engage in high-risk behavior (e.g., intravenous drug use) or in whom exposure to hepatitis B during pregnancy is suspected
 HR13 Women at high risk (see HR4) who have a nonreactive HIV test at the first prenatal visit
 HR14 Women with risk factors for intrauterine growth retardation (see HR8)

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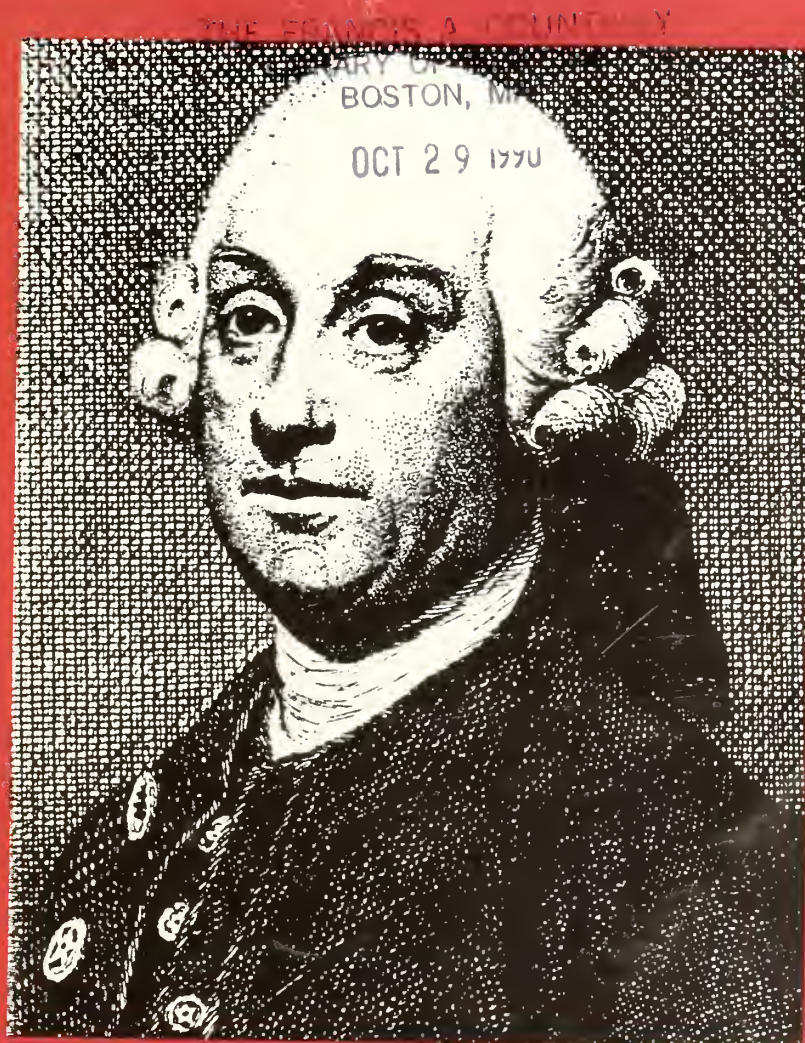
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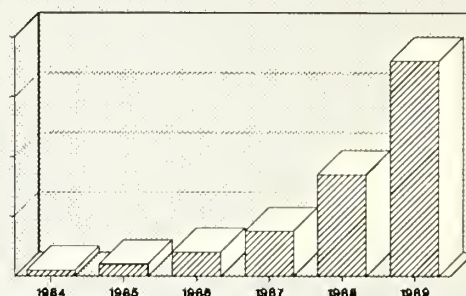


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Cover: The cover illustration is a likeness of the eminent London surgeon, Percivall Pott (1714-1788)

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The Prevention of Cancer

This issue of the *Journal* carries articles describing recent advances in the non-surgical therapies for cancer. Radiotherapy and chemotherapy have each achieved notable successes through relentless clinical testing and basic research; but while they represent critical interventions in prolonging life, 2,600 Rhode Islanders will nevertheless die of cancer this year. Indeed, these review articles emphasize repeatedly that permanent cure, as an outcome of these nonsurgical therapies, is encountered in only a fraction of cancer cases.

Cancer prevention, of course, represents the goal of all physicians concerned with the social burden of malignant disease. But if cancer is a random happenstance; if cancer strikes without cause or pathophysiologic reason, then efforts directed toward prevention become an irrelevance and a waste of time. Prevention, as a medical principle, is pointless unless we know what to prevent.

The first inroads into the mysteries of cancer etiology began about two centuries ago. Through the observations of certain eighteenth and nineteenth century clinicians, operating under the premise that most every medical effect had a cause, certain risk factors for skin cancer became apparent. In 1775, a year before the Declaration of Independence, Percival Pott published a medical text with the inelegant title, "Chirurgical Observations Relative to the Cataract, the Polypus of the Nose, the Cancer of the Scrotum, the Different Kinds of Ruptures,

and the Mortification of the Toes and Feet." About 800 words of this treatise are devoted to cancer of the scrotum. Potts notes, "It is a disease which always makes its first attack on, and its first appearance in the inferior part of the scrotum; where it produces a superficial, painful, ragged, ill-looking sore, with hard and rising edges. The trade call it the soot-wart. I never saw it under the age of puberty, which is, I suppose, one reason why it is taken, both by patient and surgeon, for venereal. . . ." He further observes, "The fate of these people (ie, chimney sweeps) seems singularly hard; in their early infancy, they are most frequently treated with great brutality, and almost starved with cold and hunger; they are thrust up narrow, and sometimes hot chimneys, where they are bruised, burned, and almost suffocated; and when they get to puberty, become peculiarly liable to a most noisome, painful and fatal disease." In terms of cause, Pott states, "The disease in these people, seems to derive its origin from a lodgment of soot in the rugae of the scrotum. . . ." With the subsequent passage of child labor laws in England, encouraged in no small measure by the work of Pott, scrotal cancer virtually disappeared.

In 1866 a Scottish physician, W. Elmslie, published a notable paper "On the Etiology of Epithelioma Among the Kashmiris." While working in a medical missionary dispensary in India, Elmslie identified 30 cases of "unmistakable epithelioma" amongst 5,080 patients. He observed that

all of these lesions were confined to the inner thigh or abdominal surfaces and he ascribed this restrictive distribution to the local custom of carrying portable braziers (called kangris), containing burning charcoal, beneath the clothing to ward off the cold. Elmslie states that the heat of the kangri acts injuriously on the skin thus giving rise to the epitheliomata. He then inductively speculates whether this association with heat might explain cancer of the lip in English pipe smokers.

About two decades later another English physician, J. Hutchinson, noted an association between arsenical therapy and subsequent skin cancer.

The notion that cancer may be prevented by first identifying its causes has now resulted in many public health measures aimed at limiting human exposure to these causes. Clinical epidemiology has yielded innumerable associations: Thus, for example, city people, consumers of certain diets, those in certain occupations and those with certain preoccupations are shown to be more likely to develop cancer than others.

Has cancer always been a human burden? Virtually all medical texts before the nineteenth century avow that cancer was quite uncommon. Admittedly, the instruments and procedures which help us to identify cancer were not around centuries ago, but certain externally located neoplasms, skin and breast, were well-known to the medical community.

Observers have therefore pon-

dered whether cancer may perhaps be a disease of civilization and its industrial components; accordingly, they have directed their scrutiny to the incidence of cancer in contemporary cultures "uncontaminated by the accoutrements of civilization." Vilhjalmur Stefansson, the eminent Arctic explorer and ethnologist was impressed with the utter rarity of cancer in Eskimos. F. Hoffman, studying native Bolivian populations in 1923, was unable to trace a single authentic case of malignant disease. Dr Albert Schweitzer wrote, "On my arrival in Gabon (Africa), in 1913, I was astonished to encounter no cases of cancer. . . . I can not, of course say positively that there was no cancer at all; but, like other frontier doctors, I can only say that if any cases existed they must have been quite rare."

An immense array of geographically-stratified cancer data has now been gathered to show that there are notable — and consistent — variations in the incidence rates of certain cancers; that some regions are virtually free of the disease while other areas have high frequencies which, in turn, are closely associated with certain identified risk factors.

While the principal etiologic factors preceding some forms of cancer are now established, there remain other common cancers, particularly breast and colon cancer, where no exogenous factors are obvious. It is likely that the field of clinical epidemiology (which has shown us the relationships between benzene and leukemia, cigarette smoking and lung cancer, industrial exposures and a host of skin, bladder and lung cancers) will eventually provide us with abundant etiologic insights so that specific preventive steps may then be adopted. The thoughtful words of Stefansson are worth recalling as we seek

answers from the accumulating cancer registry data:¹

1. Learn how men formerly lived where diligent and competent search for generations has revealed little or no cancer.

2. On the frontier, pay heed to what the changes were that took place through the several decades which preceded the first detection of cancer, and to those changes which took place thereafter during the rise of cancer toward its present dread frequency.

3. Likewise, in our cities and rural communities, observe how those groups now live who are least afflicted by cancer, and how those live that are most afflicted.

Stanley M. Aronson, MD

¹Stefansson, V. *Cancer: Disease of Civilization?* Hill & Wang Publishers, New York, 1960.

Cont. from page 443

who in 1775 described scrotal cancer in chimney sweeps and suggested that this cancer was due to the manner of employment and hence was a preventable lesion (see editorial, page 445). His other contributions to medicine include a treatise on ruptures, probably the first publication describing congenital hernias; a description of tuberculous kyphosis (Pott's disease); and the nature of certain bone fractures (Pott's fracture).

On Call

Elissa Spinner, MD

Sifting through the confusion of
sounds,
Unweaving knotted scenes,
Where am I?
Am I surfacing in the
Emergency Room
Watching your yellow and red
pen
Bobbing along the page?
Scrawling through orders: Date,
Time, Place.
Let's give fluids: By mouth? By
vein?
Apply to skin?
No, not here because I'm
Breathing through my mouth
Head flat back —
Must be floating
Past the wide wide page,
operators
Talking all night to strangers
Solid, ballast, allowing
connections
Hello? Hello?
It's time now. Now.
Delivery, time to bring Forth
Delivery.
Snap, nod and shudder,
Now this is it
Awake, O.K.? No more drifting —
With shoes on I can stay fixed
to the floor
and run.
Earthbound, I sort and shift in
forward only,
Run, it's a baby,
Now run.

* * *

This poem is printed in loving memory of its author who was tragically killed in April, 1990. Dr Elissa Spinner was a Brown University graduate, class of 1983, worked as a clinical clerk in many of the Providence community hospitals, and had received her MD from the University of Vermont. At the time of her death she was a resident physician in pediatrics at Strong Memorial Hospital, Rochester, NY. She was a gifted poet, artist and physician.



"The Wind's Highway - The Fanny Forrester"

Oil on Canvas

Montague Dawson, RSMA

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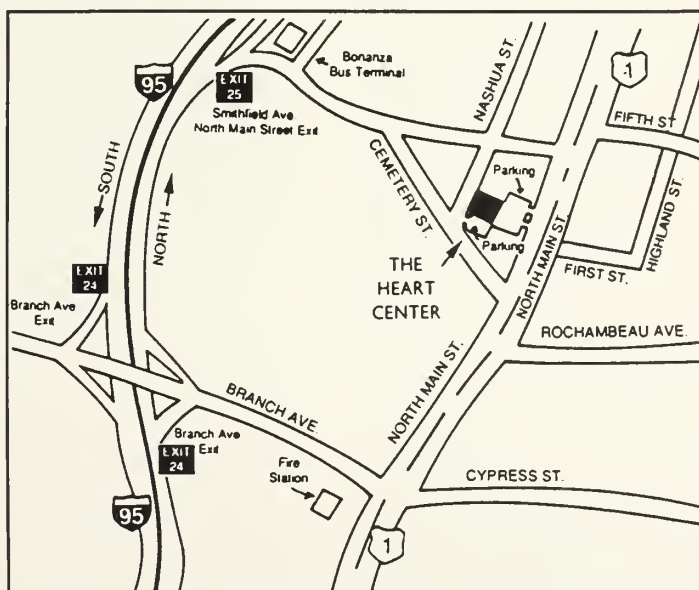
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Am Fam Phys 1987;36:133-140

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Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:

- Hypersensitivity reactions have been reported in about 1.5% of patients and include morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions have been reported with the use of Cecilor. These are characterized by findings of erythema multiforme, rashes, and other skin manifestations accompanied by arthritis/arthralgia, with or without fever, and differ from classic serum sickness in that there is infrequently associated lymphadenopathy and proteinuria, no circulating immune complexes, and no evidence to date of sequelae of the reaction. While further investigation is ongoing, serum-sickness-like reactions appear to be due to hypersensitivity and more often occur during or following a second (or subsequent) course of therapy with Cecilor. Such reactions have been reported more frequently in children than in adults with an overall occurrence ranging from 1 in 200 (0.5%) in one focused trial to 2 in 8,346 (0.024%) in overall clinical trials (with an incidence in children in clinical trials of 0.055%) to 1 in 38,000 (0.003%) in spontaneous event reports. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy; occasionally these reactions have resulted in hospitalization, usually of short duration (median hospitalization = two to three days, based on postmarketing surveillance studies). In those requiring hospitalization, the symptoms have ranged from mild to severe at the time of admission with more of the severe reactions occurring in children. Antihistamines and glucocorticoids appear to enhance resolution of the signs and symptoms. No serious sequelae have been reported.
- Stevens-Johnson syndrome, toxic epidermal necrolysis,

and anaphylaxis have been reported rarely. Anaphylaxis may be more common in patients with a history of penicillin allergy.

- Gastrointestinal (mostly diarrhea): 2.5%
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1% and, rarely, thrombocytopenia and reversible interstitial nephritis.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient lymphocytosis, leukopenia, and, rarely, hemolytic anemia and reversible neutropenia.
- Rare reports of increased prothrombin time with or without clinical bleeding in patients receiving Cecilor and Coumadin concomitantly.
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clintest[®] tablets but not with Tes-Tape[®] (glucose enzymatic test strip, Lilly).

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Recent Developments in Medical Oncology

William M. Sikov, MD
Robert D. Siegel, MD

Postoperative adjuvant chemotherapy in both colon cancer and node-negative breast cancer are prime examples of newly accepted elements in the overall treatment plan of patients with these diseases.

The recent development of new drugs and treatment strategies in the therapy of many common cancers has created an expanding role for the medical oncologist. Postoperative adjuvant chemotherapy in both colon cancer and node-negative breast cancer are prime examples of newly accepted elements in the overall treatment plan of patients with these diseases. In prostate cancer, the release of several new hormonal agents has provided a wide range of alternatives in the treatment of advanced disease. This review will focus on these new developments and their impact. Despite these advances, there remain unanswered ques-

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tions. Many of these questions are being addressed by clinical studies available locally. Participation of all appropriate patients in these studies should be encouraged.

Treatment of Node-Negative Breast Cancer

Perhaps the most significant controversy to develop during the past one to two years in medical oncology has been the conflict over the appropriate post-operative treatment of patients with breast cancer and negative axillary lymph nodes. The use of post-operative adjuvant systemic therapy is based on the premise that distant micrometastatic disease may already exist at the time of diagnosis which would be unaffected by any therapies, such as surgery or radiation therapy, directed solely at the breast and axilla. Clearly, the risk of occult metastases is higher in those patients whose axillary lymph nodes are involved by tumor than in those whose axillary nodes are negative.

Several randomized studies have demonstrated the efficacy of systemic adjuvant therapy in node-positive patients, and the use of post-operative treatment in

this patient group has become routine. A National Cancer Institute (NCI) Consensus Conference held in 1985 endorsed the use of systemic chemotherapy for all premenopausal patients with positive lymph nodes, and tamoxifen therapy for post-menopausal women whose tumors were node-positive and hormone receptor positive.¹ However, approximately 70% of patients with node-negative breast cancer will be alive 10 years after surgery without relapse. At the time of the 1985 Consensus Conference, there was

ABBREVIATIONS USED:

CMFP: cyclophosphamide, methotrexate, 5-fluorouracil, prednisone

DES: diethylstilbesterol

DNA: deoxyribonucleic acid

5-FU: 5-fluorouracil

LHRH: luteinizing hormone releasing hormone

MOF: methyl-CCNU, oncovin, 5-FU

NCCTG: North Central Cancer Treatment Group

NCI: National Cancer Institute

NSABP: National Surgical Adjuvant Breast and Bowel Project

felt to be insufficient evidence to warrant recommending the routine use, outside of a clinical trial, of any adjuvant modality in this patient group, most of whom are cured by their primary treatment (ie, breast surgery with or without radiation).

The recent publication of several studies evaluating the efficacy of adjuvant treatment of node-negative breast cancer has prompted a reevaluation of the conclusions of the 1985 Consensus Conference and has been a source of considerable disagreement within the medical oncology community. The three most quoted studies include two from the National Surgical Adjuvant Breast and Bowel Project (NSABP B-13 and B-14) and one Intergroup study. All three studies included a no treatment control arm.

NSABP B-13 evaluated 679 patients with node-negative breast cancers whose tumors were also negative for estrogen receptors.² The patients were randomized to receive either no therapy or chemotherapy with methotrexate and 5-FU. At four years, 80% of the treated patients remained free of disease compared with 71% of the control group, a statistically significant difference. NSABP B-14 randomized 2,644 patients with estrogen receptor positive, node-negative tumors between adjuvant tamoxifen and no therapy.³ Again, there was a statistically significant decrement in the relapse rate in the treatment arm with 82% of tamoxifen treated patients remaining disease-free at four years compared with 77% of those untreated. Finally, the Intergroup study included 536 node-negative patients with either estrogen receptor negative tumors or estrogen receptor positive tumors measuring ≥ 3 cm.⁴ Patients were randomized to treatment with cyclophosphamide, metho-

trexate, 5-fluorouracil and prednisone (CMFP) or observation alone. Eighty-one percent of the CMFP treated group remained relapse-free at 5 years compared to 58% of the observation group, the largest differential of the three studies. Despite the improvements in disease-free survival seen in all three studies, none has yet demonstrated an overall survival advantage for the various treatments. Proponents of these studies feel that with continued follow-up, a survival advantage will eventually develop as patients currently relapsing ultimately succumb to their disease.

These studies are, however, not without their detractors. First, the publicity associated with the release of these data has perhaps unintentionally created an atmosphere in which both physicians and patients with node-negative breast cancer feel that some form of treatment is an imperative. In fact, many women will have clinically occult tumors demonstrated mammographically which are too small for standard quantitative assays for estrogen receptors. Such patients were not included in the above named studies and therefore the results are not necessarily applicable to them. Second, patients with node-negative breast carcinoma have a relatively favorable prognosis even without adjuvant therapy. Some have questioned whether exposing all such patients to the toxicity of chemotherapy (albeit mild) or the as yet undefined consequences of long-term tamoxifen use, in addition to the expense of treating all women with node-negative tumors, is worth the small improvements in disease-free survival noted in some studies. The continuing development of tumor DNA flow cytometry and analysis of protooncogenes may help to select those node-negative pa-

tients at highest risk of relapse and thereby target adjuvant therapies to this group alone.⁵ Those felt to be at highest risk may even be candidates for more intensive adjuvant therapy. Finally, many feel that dissemination of the results of these studies was premature and the improvements in disease-free survival may not translate into improvements in overall survival if these treatments merely delay but do not prevent relapse.

Despite these raging debates, there are several points on which most researchers agree. There are a variety of national studies actively investigating both the optimal adjuvant therapy of and prognostic factors in node-negative breast carcinoma. These protocols are available at several Rhode Island hospitals. Whenever possible, participation of appropriate patients in these studies remains a high priority. Virtually all investigators also caution against generalizing the results of recently published studies to women with small, clinically occult, mammographically documented breast cancers. There are studies addressing the appropriateness of adjuvant therapy in this group of patients, and these women should probably not be routinely treated outside the setting of a protocol.

There remains some debate as to the appropriateness of adjuvant therapy in node-negative breast cancer. Many oncologists seem to share the notion that "the burden of proof is now on the physician and patient as to why an individual patient should not receive some form of adjuvant therapy."⁶ However, there is not universal acceptance of this concept and only continued support of ongoing clinical research projects will help end the controversy.

Adjuvant Therapy for Colon Cancer

Developments in the past year have revived hopes for improving the prognosis for patients with locally advanced adenocarcinoma of the colon. Of the approximately 150,000 new cases diagnosed annually in the United States, most are discovered at a stage of disease where surgical resection with curative intent is possible. Unfortunately, disease recurrence due to micrometastases outside the surgical field limits 5-year survival to 60-70% in patients whose disease extends to or through the bowel serosa (Dukes' Stage B) and 30-40% in patients with local lymph node involvement (Dukes' C).

Adjuvant therapy to reduce the failure rate has been studied for over 30 years. Its development has been handicapped by the absence of effective chemotherapeutic agents against colon cancer. The most effective single agent in advanced disease is 5-fluorouracil (5-FU), with a partial response rate of 15-20%. Alone, and in combination with other marginally active agents, 5-FU has been tested extensively to determine if its use in the adjuvant setting can improve the surgical cure rate. In several studies, no treatment benefit has been demonstrated for 5-FU alone.^{7,8} A single large study from the National Surgical Adjuvant Breast and Bowel Project (NSABP) did demonstrate significant improvements in disease-free survival and overall survival for stage B and C patients receiving postoperative semustine, vincristine, and 5-FU (MOF) chemotherapy compared to untreated controls.⁹ However, several other trials have failed to confirm the efficacy of semustine and 5-FU chemotherapy in the adjuvant setting.^{7,8}

The mechanism of 5-FU activity is believed to be inhibition of DNA

synthesis by competitive binding of the active form of the drug, 5-FdUMP, to thymidylate synthetase (TS), and its efficacy is limited by dissociation of the 5-FdUMP: TS complex. The presence of reduced folates, such as folinic acid, also known as leucovorin or citrovorum factor, stabilizes the complex, enhancing 5-FU cytotoxicity. In advanced colon cancer, administration of folinic acid increases the response rate of 5-FU to 20-50%, though whether this prolongs overall survival is controversial.⁸ Hematologic and especially gastrointestinal toxicity are increased in patients receiving the 5-FU/folinic acid combination with a disturbing incidence of profuse diarrhea in elderly patients. Controlled studies of this combination as adjuvant therapy are underway, but for the major US study, a joint project of several cooperative groups, accrual to the no treatment arm was prematurely terminated after publication of a recent study on the role of 5-FU and levamisole as adjuvant agents.

Levamisole is an antihelminthic agent widely used in humans and domesticated animals in the Third World. In the 1970s, it was found to have immunostimulatory properties, including T-cell activation and enhancement of macrophage function. While *in vitro* levamisole alone or in combination with 5-FU inhibits the growth of colon cancer lines only at concentrations well above those achievable in humans, a non-randomized trial of levamisole in colon cancer following tumor resection suggested a possible improvement in survival, presumably related to immunologic activation. Thus, the North Central Cancer Treatment Group (NCCTG) and the Mayo Clinic initiated a randomized study of levamisole in an adjuvant role.¹⁰ Four hundred and one patients with

poor prognosis stage B (tumor invading into or through the serosa, with or without involvement of pericolic or perirectal fat, or invading adjacent organs by direct extension) or stage C cancer of the colon or rectum were assigned to receive no postoperative therapy, levamisole alone, or levamisole plus 5-FU. With a minimum follow-up of over 4 years, both the levamisole alone arm and the levamisole plus 5-FU arm exhibit reductions in the rate of recurrence of approximately 30%. This results in a 5-year recurrence-free rate of 58% for treated patients versus 48% for untreated controls, a significant improvement, though, for the group as a whole, treatment has not significantly affected overall survival.

Levamisole is an antihelminthic agent widely used . . . in the Third World. In the 1970s it was found to have immunostimulatory properties including T-cell activation . . .

When the patients are divided by stage, the stage C patients who had been treated with 5-FU and levamisole postoperatively exhibited significant improvement in both freedom from recurrence and overall survival compared to controls. For stage B patients, differences did not achieve statistical significance, which may be due to the relatively low risk of recurrence for untreated patients in this group. Toxicity with levamisole alone was minimal, while patients receiving levamisole plus 5-FU had moderate hematologic and gastrointestinal toxicity with no treatment-related deaths.

These results were confirmed by a subsequent, much larger, intergroup study.¹⁷ For 318 Stage B patients assigned to receive either no postoperative therapy or lev-

amisole plus 5-FU, while there have been fewer recurrences at 3 years in the treated group, there is as yet no significant difference in disease free survival or overall survival. For 929 Stage C patients, 63% of patients treated with levamisole plus 5-FU were free of disease at 3½ years compared to 47% of patients receiving no post-operative therapy, a 33% reduction in the death rate. Therapy with levamisole alone produced no detectable improvement in disease-free survival or overall survival. Toxicity of levamisole plus 5-FU therapy was similar to what might have been anticipated with 5-FU alone, including nausea, vomiting, diarrhea, stomatitis, dermatitis, and leukopenia, all of which were rarely severe. There was only one treatment-related death, this due to profound leukopenia and sepsis.

... stage C patients (with colon cancer) who have been treated with 5-FU and levamisole postoperatively exhibited significant improvement in both freedom from recurrence and overall survival ...

A smaller British study demonstrated improved freedom from recurrence for patients treated with levamisole plus 5-FU compared to patients receiving no adjuvant therapy or 5-FU alone.¹² A European study failed to show recurrence or survival benefits from levamisole alone compared to a placebo control group.¹³ With these as background, two large studies comparing 5-FU/folinic acid, 5-FU/levamisole, and 5-FU/levamisole/folinic acid as adjuvant therapy in stage B and C patients have been organized, one sponsored by the NSABP and the other a joint study involving several cooperative groups.

Though reasonably well toler-

ated, the adjuvant therapies listed above involve considerable expense and inconvenience compared to observation alone, leading some to question the cost: benefit ratio of such therapy. Furthermore, initial positive studies of levamisole as adjuvant therapy in breast cancer, non-small cell lung cancer, and melanoma could not be confirmed in subsequent studies. Only further study can determine the true role of new adjuvant therapies for colon cancer, including the optimal dose and timing of the agents used. Thus, while levamisole is available for use outside a clinical trial, eligible patients should be strongly encouraged to enroll in studies which are available at several hospitals in Rhode Island. Over the next several years, these studies should reveal whether progress is being made towards controlling this common malignancy.

New Therapies for Prostate Cancer

Almost 50 years ago, Huggins and Hodges demonstrated that prostate cancer manifests marked androgen dependence for growth.¹⁴ Since that time, hormonal manipulation aimed at androgen deprivation has been the mainstay of therapy for patients with advanced disease. There are currently several new products available for use in advanced prostatic cancer. Many of these products have novel mechanisms of action and may provide equivalent or slightly better results than older therapies with less toxicity.

The testis is the source of 95% of circulating androgens while the adrenal glands supply the remainder. In the past, androgen lowering therapies have been aimed predominantly at the testis. Orchiectomy remains the simplest and probably most cost-effective method to permanently decrease serum testosterone lev-

els. It almost routinely results in impotence. Estrogen therapy usually in the form of diethylstilbestrol (DES) has been a reasonable alternative to orchiectomy for those patients unwilling to undergo surgery. DES acts by interfering with the normal hypothalamic-pituitary-testicular axis and results indirectly in the lowering of serum testosterone to castrate levels. Estrogen administration, however, has been linked to increased thromboembolic phenomena and cardiovascular events which limits its usefulness in elderly men with comorbid medical conditions.

... hormonal manipulation aimed at androgen deprivation has been the mainstay of therapy for patients with advanced prostatic cancer.

Two classes of drugs, leuteinizing hormone releasing hormone (LHRH) analogues and antiandrogens, have been approved in the past 5 years for use in patients with advanced prostate cancer. The LHRH analogues, such as leuprolide, when administered subcutaneously on a daily basis, provide a supraphysiologic stimulus to the pituitary which ultimately suppresses the secretion of gonadotropins. In effect, this results in a medical hypophysectomy decreasing serum testosterone to castrate levels due to the lack of circulating gonadotropins. LHRH analogues can induce a brief surge in gonadotropin (and therefore testosterone) secretion initially, sometimes clinically manifested as a "flare" of symptoms during the first 1-2 weeks of therapy.

Leuprolide has been compared to DES in a multi-institutional randomized study of patients with metastatic prostate carcinoma.¹⁵ The drugs produced equivalent

survival and response data. However, the DES patients experienced significantly more painful gynecomastia, nausea and vomiting, edema, and thromboembolic events than did those taking leuprolide. The leuprolide group did experience "hot flashes" more frequently. LHRH analogues therefore appear to be therapeutically equivalent to DES with less toxicity, albeit more expensive. The recent release of depot forms of LHRH analogues that allow monthly rather than daily injections may make this alternative even more attractive.

Antiandrogens represent another addition to the armamentarium for the treatment of prostate cancer. This class of agents is exemplified by flutamide, a drug recently released for use in prostate cancer. Flutamide is an oral nonsteroidal agent which acts by inhibiting the binding of androgens to their cytoplasmic receptor. Unlike other agents, flutamide does not decrease the production of androgens, and serum testosterone is frequently normal during treatment. A postulated advantage of this class of agents is that they inhibit the effect of androgens regardless of whether they originate from the testis or adrenal gland.

A recent study evaluated whether treatment with both leuprolide and flutamide conferred any advantage over treatment with leuprolide alone.¹⁶ The hypothetical basis of the combination was to provide total androgen blockade by both reducing gonadal androgens (leuprolide) and inhibiting the effects of adrenal androgens at the cellular level (flutamide). The combination provided a small but statistically significant improvement in both median time to progression of disease (16.5 vs 13.9 months) and death (35.6 vs 28.3 months). In addition, the concurrent use of

flutamide seemed to minimize the leuprolide-induced "flare." The only additional toxicity of flutamide was mild diarrhea. A question unanswered by this study is whether leuprolide is necessary at all in patients receiving flutamide. In small uncontrolled studies, flutamide alone has demonstrated a level of efficacy similar to other established hormonal manipulations, but with a lower incidence of impotence.¹⁷ This should be further evaluated in larger randomized trials.

Despite the development of new treatments, advanced prostate cancer remains an incurable disease. Bilateral orchiectomy remains the treatment of choice when complications of the disease (spinal cord compression, bilateral ureteral obstruction) require prompt treatment. However, in less emergent situations, newer (and more expensive) therapies can provide a level of palliation similar to or perhaps slightly better than older therapies without the psychological and minimal surgical morbidity of orchiectomy or the toxicity of DES. Although newer therapies are effective treatment alternatives, none are yet able to provide a level of disease control substantially better than older interventions.

References

- ¹ NIH Consensus Conference: Adjuvant Therapy for Breast Cancer. *JAMA* 1985;254:3461-3463.
- ² Fisher B, Redmond C, Dimitrov NV, et al. A Randomized Clinical Trial Evaluating Sequential Methotrexate and Fluorouracil in the Treatment of Patients with Node-Negative Breast Cancer who have Estrogen-Receptor-Negative Tumors. *N Engl J Med* 1989;320:473-478.
- ³ Fisher B, Costantino J, Redmond C, et al. A Randomized Clinical Trial Evaluating Tamoxifen in the Treatment of Patients with Node-Negative Breast Cancer who have Estrogen-Receptor-Positive Tumors. *N Engl J Med* 1989;320:479-484.
- ⁴ Mansour EG, Gray R, Shatila AH, et al. Efficacy of Adjuvant Chemotherapy in High-Risk Node-Negative Breast Cancer. An Intergroup Study. *N Engl J Med* 1989;320:485-490.

- ⁵ Clark GM, Dressler LG, Owens MA, Pounds G, Oldaker T, McGuire WL. Prediction of Relapse or Survival in Patients with Node-Negative Breast Cancer by DNA Flow Cytometry. *N Engl J Med* 1989;320:627-633.
- ⁶ Glick JH. Meeting Highlights: Adjuvant Therapy for Breast Cancer. *J Natl Cancer Inst* 1988;80:471-475.
- ⁷ Buyse M, Zeleniuch-Jacquotte A, Chalmers TC. Adjuvant Therapy of Colorectal Cancer. Why we still don't know. *JAMA* 1988;259:3571-3578.
- ⁸ Mayer RJ, O'Connell MJ, Tepper JE, Wolmark N. The Status of Adjuvant Therapy for Colorectal Cancer. *J Natl Cancer Inst* 1989;81:1359-1364.
- ⁹ Wolmark N, Fisher B, Rockette H, et al. Postoperative Adjuvant Chemotherapy or BCG for Colon Cancer: Results from NSABP Protocol C-01. *J Natl Cancer Inst* 1988;80:30-36.
- ¹⁰ Laurie JA, Moertel CG, Fleming TR, et al. Surgical Adjuvant Therapy of Large Bowel Carcinoma: An Evaluation of Levamisole and the Combination of Levamisole and Fluorouracil. *J Clin Oncol* 1989;7:1447-1456.
- ¹¹ Moertel CG, Fleming TR, MacDonald JS, et al. Levamisole and Fluorouracil for Adjuvant Therapy of Resected Colon Carcinoma. *N Engl J Med* 1990;322:352-8.
- ¹² Windle R, Bell PRF, Shaw D. Five Year Results of a Randomized Trial of Adjuvant 5-Fluorouracil and Levamisole in Colorectal Cancer. *Br J Surg* 1987;74:569-572.
- ¹³ Arnaud JP, Buyse M, Nordlinger B, et al. Adjuvant Therapy of Poor Prognosis Colon Cancer with Levamisole: Results of an EORTC Double-Blind Randomized Clinical Trial. *Br J Surg* 1989;76:284-289.
- ¹⁴ Huggins C, Hodges CV. Studies on Prostatic Cancer. I. The Effect of Castration, of Estrogen, and of Androgen Injection in Metastatic Carcinoma of the Prostate. *Cancer Res* 1941;1:293-297.
- ¹⁵ The Leuprolide Study Group. Leuprolide versus Diethylstilbesterol for Metastatic Prostate Cancer. *N Engl J Med* 1984;311:1281-1286.
- ¹⁶ Crawford ED, Eisenberger MA, McLeod DG, et al. A Controlled Trial of Leuprolide with and without Flutamide in Prostatic Carcinoma. *N Engl J Med* 1989;321:419-424.
- ¹⁷ Sogani PC, Vagaiwala MR, Whitmore WF. Experience with Flutamide in Patients with Advanced Prostatic Cancer without Prior Endocrine Therapy. *Cancer* 1984;54:746-750.

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Rhode Island Patients Undergoing Outpatient Chemotherapy

Vincent Mor, PhD
Susan Masterson-Allen, MA

This paper . . . will provide readers with an impression of the difficulties with which patients undergoing outpatient treatment, and their families, must cope.

Cancer patients are a vulnerable population. Their vulnerability is heightened by their treatment experience, particularly if treatment is administered on an outpatient basis. Although recovery from the psychological trauma of treatment may be expedited by the familiarity and comfort of one's family and home surroundings, physiological side effects may interfere with the performance of routine activities.^{1,2} Inability to perform these activities can result in noncompliance with treatment regimens, and ultimately, may compromise health status.³

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While many patients have informal support systems that are both willing and able to meet needs arising from the disease and its treatment, help is not always readily available. Similarly, the fragility of some informal support systems limits their ability to provide a level of care that is adequate to meeting a complex of patient needs.^{4,5}

In recognition of the increasing trend toward out-of-hospital cancer treatment, the National Cancer Institute launched an initiative to determine the extent to which this shift in the locus of care creates problems for patients and their families at home. The Center for Gerontology and Health Care Research, Brown University Program in Medicine, was awarded two grants related to this initiative. The first of these grants, "Cancer Patients' Concrete Service Needs," was a two-phase study designed to first, identify risk factors for inadequate assistance with daily living needs among cancer patients receiving chemotherapy on an outpatient basis, and second, to design and test a case-management intervention that would educate patients and their families concerning community resources

available to assist with their needs. Each phase of the "Concrete Needs" study accrued a separate sample of cancer patients.

A second grant, "Cancer Patients' Home Care Needs and Costs," was a longitudinal study conducted in three geographic settings: Rhode Island, New York City and Central Pennsylvania. The goals of this study were to determine the level of need among patients receiving outpatient chemotherapy and radiation treatment, the extent to which this need was met by formal and informal sources, and the extent of burden experienced by caregivers in the home setting.

Patients were accrued from hospital-based clinics and private practices in Rhode Island for both phases of the "Concrete Needs" study and for the "Home Care" study. This paper will report baseline patient survey results on outcome measures which are common to the three studies in question, focusing on measures which will provide readers with an impression of the difficulties with which patients undergoing outpatient treatment, and their

ABBREVIATIONS USED:

ADL: activities of daily living

families, must cope. We will confine our discussion to patients receiving outpatient chemotherapy treatment in Rhode Island, in order to examine the differences and similarities in findings across three relatively homogeneous samples of cancer patients.

Study Methodologies

Concrete Needs Phase 1 All patients over the age of 21 in active cancer-related chemotherapy or hormonal treatment on an out-patient basis were considered eligible. Chemotherapy for solid tumor cancers as well as leukemia and lymphoma met study criteria as cancer-related treatment.

Participating sites included the major oncology clinics and private practices in Rhode Island. All patients referred by these sites were randomly assigned to research interviewers who contacted patients, explained the study, and requested participation. Patients were interviewed as soon as possible after study entry. All interviews were conducted over the telephone. Subsequent to the initial assessment, disease and treatment characteristics were abstracted from patients' medical records.

Concrete Needs Phase 2 Patients eligible for participation in Phase 2 were Rhode Island residents at least 21 years old who were initiating a *new* course of outpatient chemotherapy. Patients diagnosed with solid tumors or with leukemia or lymphoma were accepted into the sample. Patients receiving hormonal treatment only were not eligible for the study since it was found in Phase 1 that this treatment did not have a profound affect on physical functioning and, therefore, on concrete service needs. Patient accrual protocol and baseline interview data collection proceeded as in Phase 1.

Home Care Study Patient eligibility criteria were selected to target those patients who were likely to experience functional decline as a consequence of treatment or disease progression, yet who had a reasonable chance of surviving 6 months post-initiation of treatment. Eligible cases were those patients aged 21 or older with non-localized, recurrent, or inoperable neoplastic disease whose primary disease sites involve solid tumors of the gastrointestinal tract, genitourinary tract, breast, lung (all stages), and head and neck. In addition, patients with Hodgkin's disease and non-Hodgkin's lymphoma were eligible.

In Rhode Island, patients were identified at two hospital-based chemotherapy clinics. Following patient identification, patients were mailed a letter explaining the study and were contacted by phone within 30 days of study entry. In addition, disease and treatment-related information was abstracted from patients' medical records at 6 months post-baseline.

Patient Assessment

In addition to basic demographic data (eg, sex, age, education, race, marital status, living arrangements, and employment status), patient interviews in all three studies contained the following domains in common:

1. *Utilization of health care services*, including the number of hospitalizations and number of emergency room visits in the 3 months preceding interview contact, and the number of physicians seen regularly.

2. *Formal and informal sources of assistance* to meet daily living needs (eg, family, friends, formal service agency).

3. An assessment of *daily living needs* conceptualized as necessary for community-based liv-

ing were grouped into the following domains of need: *Physical* (ability to bathe and transfer); *Instrumental* (cooking, light and heavy housekeeping, shopping, transportation to the doctor and transportation for other purposes); *Home Health* (medical tasks); and *Administrative* (completion of forms and paperwork such as insurance claims and applications for entitlements, financial counseling, legal counseling, information about cancer and relevant treatment).

Conditions of a patient having no need for assistance, met need, and unmet need were defined as follows: *no need* is defined as a patient performing an activity alone, and no further help is needed; *met need* is defined as a patient having help in performing an activity, and reporting that the help received is sufficient; *unmet need* is defined as patients performing an activity alone when they need help, or having help but reporting they need more help.

4. *Presence and severity of symptoms* experienced in the 2 weeks before interview.

5. *Disruption caused by treatment*, including the overall difficulty of the treatment experience, disruption in daily routine, reduction in contact with family and friends, and reduction in social activities.

Results Across Studies

Study Samples Sociodemographic and disease-related characteristics of the three study samples are presented in Table 1. Patient samples are fairly similar demographically, with some variations that are probably attributable to differences in the distribution of patients with various cancer types and stages. For example, the large proportion of patients in the Home Care Study with advanced disease may account for the lower proportion who were

Table 1. Description of Study Samples

	Home Care N= 85	Concrete Needs	
		Phase 1 N=412	Phase 2 N=301
Male	32.9%	28.6%	36.9
Patient Age			
21-44	18.8	13.6	19.3
45-64	48.2	43.2	46.5
65+	32.9	43.2	34.2
Education			
< High School	25.9	26.9	28.6
High School	41.2	35.7	35.5
Some College	9.4	15.6	15.9
College Graduate	14.1	8.8	11.6
Post-graduate	9.4	13.0	8.3
Lives Alone	12.9	20.0	17.4
Married	65.9	62.6	69.4
Employed	23.5	32.8	31.2
Primary Cancer Site			
Head/Neck	1.2	3.2	3.7
Gastro-intestinal	16.5	11.9	24.7
Lung	2.4	6.6	9.0
Breast	31.8	47.3	39.1
Genito-urinary	17.6	9.5	5.7
Hodgkins/Lymphoma	30.6	11.2	10.0
Brain	0.0	1.2	3.7
Other	0.0	9.2	4.0
Extent of Disease			
Metastatic	57.6	30.3	53.2
Regional	41.2	38.1	32.8
Local	1.2	20.1	14.0
Unknown	0.0	11.4	0.0
Number of Days in Bed			
Last 2 weeks			
0	64.7	77.2	63.4
1-3	20.1	9.5	17.1
4-13	8.2	6.7	11.7
14	7.1	6.6	7.8
Number of Days Reduced			
Activity Last 2 weeks			
0	39.3	54.7	42.0
1-3	15.6	10.2	12.8
4-13	27.6	16.6	27.8
14	17.9	18.4	17.5

employed or who lived alone at baseline. However, indicators of mobility are similar for Home Care patients and Concrete Needs Phase 2 patients, eg, 65% and 63%, respectively, report no days spent in bed in the 2 weeks before interview. Mobility is somewhat higher for Concrete Needs Phase 1 patients (77% report no bed days).

Distribution of cancer type varies somewhat across studies, with a higher proportion of Hodgkin's disease and lymphoma in the Home Care Study, a higher pro-

portion of breast cancer patients in Concrete Needs Phase 1, and more patients with cancers of the gastro-intestinal tract in Concrete Needs Phase 2. Distributions of patient age, education and marital status are roughly similar.

Statistics on health service utilization before baseline interview are presented in Table 2. As can be seen, need for home health services is fairly low, although somewhat higher for Home Care patients than for patients in the Concrete Needs studies. A higher proportion of patients in the Con-

crete Needs studies had home health needs met by formal agency use than did patients in the Home Care Study. Receipt of chemotherapy at home is rare (< 5%) across all 3 studies.

Hospitalizations in the 3 months before interview are most frequent among Concrete Needs Phase 2 patients, with fully two thirds (66%) of the sample reporting at least one hospitalization. The reverse situation is seen for Phase 1, with 65% of the sample reporting no hospitalizations. The highest percentage of patients reporting multiple hospitalizations are Home Care Study patients (23%). Use of the emergency room was much less frequent, with the majority of patients in all three studies reporting no emergency room visits in the 3 months before interview.

Patients in the Home Care Study were not asked about the number of doctors they see regularly. However, patients in both phases of the Concrete Needs study reported high physician utilization. Only a minority of patients in both studies reported seeing only one physician regularly (12% and 16%), and approximately one third of patients in both studies reported seeing four or more physicians on a regular basis (35% and 31%).

Patient Need for Assistance

Levels of patient need for assistance, both met and unmet, are reported by task in Table 3. The majority of patients in all three studies are independent in basic ADL tasks. Even in the Home Care Study, in which the majority of patients have metastasized disease, only approximately 14% of patients report needing assistance with bathing or moving in and out of bed. However, a substantial proportion of patients reporting needs report that their need is unmet (one third to one half of patients in need, across studies).

Table 2. Utilization of Health Care Services

	Home Care N = 85	Concrete Needs Phase 1 N = 412	Concrete Needs Phase 2 N = 301
Primary Source Home			
Med Care is Formal			
No	11.8%	4.1%	2.7%
Yes	3.5	6.6	6.6
NA/No need	84.7	89.3	90.7
Primary Source Home			
Chemo Care is Formal			
No	0.0	0.5	0.3
Yes	3.5	0.2	0.7
NA/No Need	96.5	99.3	99.0
Hospitalizations			
Past 3 Months			
0	42.4	65.0	34.0
1	35.3	19.2	51.0
2+	22.5	15.9	15.0
ER Visits			
Past 3 Months			
0	67.1	83.9	75.3
1	22.4	13.9	23.5
2+	10.7	2.2	1.2
Number of MDs			
Seen Regularly			
1	n/a	11.9	15.9
2	n/a	25.2	21.7
3	n/a	27.7	31.4
4+	n/a	35.1	31.1

The low level of need with ADL tasks is in sharp contrast to the relatively high level of need for assistance with Instrumental Activities of Daily Living, eg, meal preparation, housework and shopping. More than half of the patients in all studies report needing help with these tasks. Need for help with heavy housework and shopping is especially high, with 70-80% of patients in all studies requiring some assistance. As can be seen, the majority of need for instrumental activities is met.

Patients in all studies report approximately twice the need for assistance in transportation to the doctor than they do for transportation for other reasons. The majority of this need is met. As mentioned previously, need for home health services is low, and virtually all expressed need is met.

Approximately one third of patients across studies report need for assistance in filling out forms,

eg, insurance claims and applications for financial assistance. Unmet need for this assistance is somewhat higher in the Home Care Study than in either phase of the Concrete Needs study, with 10% of Home Care patients reporting not having enough help. Similarly, levels of overall need and unmet need for financial advice and legal advice are higher for patients in the Home Care Study than in the Concrete Needs Study.

More than half of the patients . . . reported needing help . . . Need for help with heavy housework and shopping is especially high . . .

Finally, patient-reported need for disease information is substantially higher in the Home Care Study than in the Concrete Needs Studies, and the proportions of patients in all studies who have

need in this area and who report that the need is not met is fairly high.

Symptom Experience Patient-reported experience of symptoms in the 2 weeks before interview is reported in Table 4 as a function of symptom severity. The most frequently reported symptom by patients in all three samples is pain (40-50%) and a substantial proportion of patients reporting pain state that it is moderate or severe.

Nausea is next in prevalence, as may be expected, given that these are samples of patients undergoing chemotherapy treatment. The prevalence of nausea is particularly high in Concrete Needs Phase 2, reported by more than half of the sample (53%). Again, substantial proportions of patients with this symptom experience it to a moderate or severe degree.

Similar proportions of patients in the three studies report diarrhea (20-26% across studies), bleeding (9-13%), fever (8-10%), shortness of breath (19-32%) and swelling (14-23%). However, while bleeding and fever are more often reported as mild, the remaining symptoms are as likely or more likely to be reported as moderate or severe.

Treatment Disruption Most patients report the experience of outpatient chemotherapy treatment as interfering in their daily lives. Approximately two-thirds of patients report that their current treatment is difficult, and one quarter report that it is very difficult (Table 5). Approximately one-third of patients in the Concrete Needs studies, and over 40% of Home Care patients, report that treatment is somewhat or very disruptive to their daily routine. While a minority of patients (11-22% across studies) report that treatment reduces social contacts somewhat or very much, higher

proportions (33-40% across studies) report that it reduces participation in social activities somewhat or very much.

Discussion

We examined need for assistance with daily activities, symptom experience, and life disruption caused by treatment across three samples of cancer patients undergoing outpatient chemotherapy in Rhode Island. Although there is some variation as a result of differences in cancer type, stage of disease and type of treatment received (ie, single vs combination chemotherapy vs hormonal therapy, as well as differences in drug type), there is enough commonality in results to assure the reliability of our findings.

Most patients report the experience of outpatient chemotherapy as interfering in their daily lives.

Since the majority of patients in these samples are not in the terminal phase of illness, we see relatively low levels of complete dependence, or need for assistance, with basic activities of daily living. In other words, most of these patients are still able to bathe themselves and to get from bed to chair without help. However, the majority of patients in all three samples reported needing assistance with more complicated and strenuous tasks such as cooking and housekeeping, or for activities that require leaving home, eg, shopping and transportation to doctor. While many of these patients will regain the ability to perform activities alone once treatment has ended, this study provides evidence that the treatment period is characterized by substantial dependence on others for the fulfillment of daily living needs. Given that the prevalence of symptoms most often

Table 3. Patient Needs at Baseline

	Home Care N = 85	Concrete Needs Phase 1 N = 412	Phase 2 N = 301
Bathing			
No Need		86.8%	88.7%
Met Need	(bathing and	10.2	8.3
Unmet Need	mobility combined)	2.9	3.0
Mobility			
No Need	86.7	92.2	96.0
Met Need	8.4	5.6	3.3
Unmet Need	4.8	2.2	0.7
Meals			
No Need	42.9	48.5	43.5
Met Need	53.6	47.8	53.8
Unmet Need	3.6	3.7	2.7
Light Housework			
No Need	45.9	42.5	46.7
Met Need	48.2	49.4	48.7
Unmet Need	5.9	8.1	4.7
Heavy Housework			
No Need	17.6	23.3	25.1
Met Need	72.9	64.6	66.2
Unmet Need	9.4	12.0	8.7
Shopping			
No Need	22.6	33.5	30.1
Met Need	71.4	61.6	64.5
Unmet Need	6.0	4.9	5.4
Transport to Doctor			
No Need	28.2	41.7	28.0
Met Need	64.7	53.1	64.3
Unmet Need	7.1	5.2	7.7
Other Transport			
No Need	63.0	58.3	60.9
Met Need	33.3	37.0	36.8
Unmet Need	3.7	4.7	2.3
Home Health Care			
No Need	84.7	89.1	90.7
Met Need	15.3	10.5	9.3
Unmet Need	0.0	0.5	0.0
Filing Forms			
No Need	61.9	67.4	63.7
Met Need	28.6	30.2	31.7
Unmet Need	9.5	2.4	4.7
Financial Advice			
No Need	79.8	90.4	93.3
Met Need	7.1	6.6	2.4
Unmet Need	13.1	2.9	4.4
Legal Advice			
No Need	83.3	n/a	92.3
Met Need	8.3	n/a	4.3
Unmet Need	8.3	n/a	3.3
Disease Info			
No Need	45.9	89.7	75.6
Met Need	36.5	3.2	12.4
Unmet Need	17.6	7.1	12.0

associated with cancer and chemotherapy, pain and nausea, are relatively high, these findings are not surprising.

However, our research indicates that the side effects of treatment are not all physiological. For some patients, the impact of

Table 4. Symptom Experience

	Home Care N = 85	Concrete Needs Phase 1 N = 412	Phase 2 N = 301
Pain			
None	60.7%	55.3%	50.0%
Mild	27.4	14.4	18.0
Moderate/Severe	11.9	30.3	32.0
Nausea			
None	70.2	61.1	46.7
Mild	21.4	16.9	31.9
Moderate/Severe	8.3	22.0	21.4
Diarrhea			
None	82.4	80.9	73.9
Mild	11.8	8.1	12.5
Moderate/Severe	5.9	11.0	13.6
Bleeding			
None	89.4	91.0	87.1
Mild	8.2	7.3	9.8
Moderate/Severe	2.4	1.7	3.1
Fever			
None	89.4	92.4	92.2
Mild	8.2	5.4	4.7
Moderate/Severe	2.4	2.2	3.1
Shortness of Breath			
None	81.0	67.9	71.5
Mild	15.5	17.2	15.6
Moderate/Severe	3.6	15.0	12.9
Swelling			
None	85.9	77.3	83.9
Mild	7.1	9.6	6.3
Moderate/Severe	7.1	13.1	9.8

treatment on social functioning may be as traumatic as its impact on physical functioning. The daily routine which constitutes normal living is disrupted, participation in social activities is suspended, and, for a minority of patients, contact with friends and families is reduced at a time when contact may be most needed.

While the majority of needs reported by patients in these studies are met by family and friends, there are subgroups of patients whose needs go unmet. These patients are either receiving help, but not enough to meet their needs, or they are attempting to perform tasks themselves, despite functional impairment due to disease and/or treatment. Other analyses of these data reveal that unmet need arises for patients who have high levels of need for assistance, and also for patients who have deficits in their infor-

mal helping network, eg, they live alone, or have only a few helpers to assist with a multiplicity of needs.^{6,7} Patients who report that their network is not resilient, that is, they do not feel they can rely on families and friends to provide help, are also more likely to have unmet need.

The daily routine . . . is disrupted, participation in social activities is suspended, and, for a minority of patients, contact with friends and families is reduced at a time when contact may be most needed.

While the dehospitalization of oncologic treatment is likely to continue over the next decade, it is unlikely that a whole new array of benefits will be introduced to cover home care for those

undergoing outpatient treatment. The consequences for that group of patients who lack the financial resources to secure formal (paid) help, and who also lack the social support resources to secure informal help, may be serious, and may ultimately compromise their ability to comply with treatment regimens.

We feel that some of the social service resources that were accepted as necessary before cancer treatment was dehospitalized need to be made available in the outpatient setting. While many hospitals do have social service workers assigned to the outpatient clinics, the volume of patients for whom these staff have ongoing responsibility is considerable. Physicians' offices may be a better setting from which to monitor the fluctuations in needs and problems that patients and their families experience. Our data reveal that the indications of potential unmet need are easily observable: level of symptomatology and functional impairment, and whether they live alone and/or have few helpers. While more clinically sophisticated staff may be necessary for backup and referral, physicians' nursing and clerical staff can screen for problems and then direct patients to available community resources, including designated professional social service staff.

Acknowledgments:

We would like to thank the Rhode Island medical and radiation oncologists, and their dedicated nurses and staff, who participated in the Concrete Needs and/or Home Care Studies. Their cooperation was an essential contribution to the success of this research effort in identifying the difficulties experienced by patients undergoing cancer treatment.

Table 5. Treatment Disruption

	Home Care N=85	Concrete Needs Phase 1 N=412	Phase 2 N=301
Difficulty of Current Treatment			
Not at all	29.4%	38.8%	36.9%
A little	21.2	18.5	15.3
Somewhat	25.9	17.8	23.5
Very	23.5	24.9	24.3
Treatment Disrupts Daily Routine			
None	37.6	48.5	47.5
A little	20.0	15.4	18.0
Somewhat	16.5	13.5	14.9
Very	25.9	22.5	19.6
Treatment Reduces Social Contacts			
None	70.6	66.0	42.7
A little	9.4	12.0	46.3
Somewhat	11.8	10.0	5.5
Very	8.2	12.0	5.5
Treatment Reduces Social Activities			
Not at all	36.5	55.7	49.0
A little	23.5	11.0	13.3
Somewhat	20.0	7.6	12.2
A lot	20.0	25.7	25.5

References

- Grobe ME, Ahmann DL, Ilstrup DM. Needs Assessment for Advanced Cancer Patients and Their Families. *Oncology Nursing Forum*. 9:26-30, 1982.
- Wool, MS, Guadagnoli E, Thomas M, Mor V. Negotiating Concrete Needs: Short-Term Training for High Risk Cancer Patients. *Health and Social Work*, 184-195, 1989.
- Mor V, Guadagnoli E, Rosenstein R. Cancer Patients' Unmet Support Needs as a Quality of Life Indicator. In Osoba, D (Ed.) *The Effect of Cancer on Quality of Life*, CRC Press, in press.
- Mor V, Guadagnoli E, Wool, M. An Examination of the Concrete Service Needs of Advanced Cancer Patients. *Journal of Psychosocial Oncology*. 5:1-17, 1987.
- Houts, PS, Yasko JM, Kahn SB, Schelzel GW, Marconi KM. Unmet Psychological, Social and Economic Needs of Persons with Cancer in Pennsylvania. *Cancer* 58:2355-2361, 1986.
- Guadagnoli E, Mor V. The Prevalence and Correlates of Chemotherapy Outpatients' Daily Living Needs. *Journal of Community Health*, in press.
- Mor V, Masterson-Allen S, Siegel K, Houts P. Factors Influencing Need and Unmet Need for Assistance Among Cancer Patients Undergoing Outpatient Treatment, unpublished manuscript, 1990.

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ERRATUM

In the article "Standards of Medical Care for Diabetic Patients: A Panel Discussion" by Quevedo et al, which appeared in the *Rhode Island Medical Journal*, the second column, lines 17-22, of page 421 contains typographical errors which should read: "nurse-educator, a lawyer, and an epidemiologist, published the standards of care document in the May 1989 issue of *Diabetes Care*. The September issue of *Diabetes Forecast*."

We apologize for these errors.
— The editors

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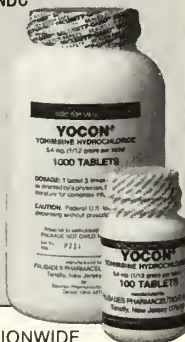
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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Recent Advances in Radiation Oncology

Roger L. Brotman, MD
Gabriela B. Masko, MD
Scott A. Triedman, MD
Banice M. Webber, MD
Anthony Yu, MD

A medical student in Philadelphia . . . hypothesized that the X-rays might also be able to "burn" cancerous tissues.

Introduction

In the latter half of 1895, an obscure German physicist, Professor Wilhelm Conrad Roentgen, was experimenting (in unrelated tests) with gas discharge tubes and fluorescent plates. Sometime in mid-November of that year, he realized that his plates were glowing, even at distances of several feet, whenever he turned on his

tubes. He came to the realization that he had discovered a new ray (which he named X) that had the ability to penetrate various substances (including those of the human body). Furthermore, he was able to capture an image of this penetration on photographic film, thus producing what he called a shadowgraph. The science of radiology was thus born. News of the discovery spread very quickly through the scientific communities of Europe, and, within 2 weeks, to the United States. During the next year, many physicians began to use the new technology to image broken bones and locate foreign bodies such as gunshot. Many of the early "radiologists" sustained skin

burns from their emerging, and poorly understood, tool.

A medical student in Philadelphia (Hahnemann Medical College . . . alma mater of one of the authors) named Emile Grubbé hypothesized that the X-rays might also be able to "burn" cancerous tissues. In an act of incredible prescience, he treated a woman with locally advanced breast cancer in January of 1896 (only 2 months after the discovery of the

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ABBREVIATIONS USED:

IORT: Intra-operative radiation therapy

RT: External beam radiation therapy

Gy: Grays (unit of radiation dose)

cGy: Centigrays (unit of radiation dose)

MeV: Million electron volts (unit of radiation energy)

NIH: National Institutes of Health

MGH: Massachusetts General Hospital

bid: Twice-a-day (radiation)

RTOG: Radiation Therapy Oncology Group

AVM: Arteriovenous malformation

CNS: Central nervous system

X-rays) and achieved a documented palliative regression. He was even able to empirically split the dose into multiple daily fractions, and to use lead shielding to protect normal tissues. Thus, the science of radiation oncology was born.

In 1898, Professors Marie and Pierre Curie in Paris discovered and characterized a distillate of pitchblende which seemed to give off natural radiation similar in properties to Roentgen's X-rays. This element was named radium. In 1901, Professor Becquerel, a colleague of the Curies, burned his chest skin after carrying a tube of radium in his vest pocket for several hours. As with Mr Grubbé 5 years earlier, Becquerel wondered whether the radium could be directly applied to a tumor to produce regression. Soon, physicians in Europe and the United States were implanting sealed tubes of radium into various human tumors (head and neck, breast and gynecologic lesions), reporting excellent results. The technique known as brachytherapy had been born.

While the early researchers made rapid progress, they were limited by the poor accuracy, precision and penetration of their equipment. In addition, they knew little about the powerful, and potentially lethal, effects of radiation on normal tissues (indeed, almost all of the "pioneers" in this field died of radiation-induced malignancies). Each decade provided major new advances: In the 1910s and 1920s, X-ray tubes became more reliable and reproducible. In the 1930s and 1940s, X-ray tubes became more powerful (penetrating) and dose measuring equipment became available. In the 1950s and 1960s, radiation oncology came into the modern age with the advent of megavoltage equipment (Cobalt 60, linear accelerators, etc.) and

specific and detailed knowledge of radiation pathology and normal tissue tolerance. The 1970s saw the beginning of particle beam applications and the beginning of the marriage of digital computers with clinical radiation therapy. This article will briefly review the newer technologies, some of which are still experimental and some of which are being used in daily clinical practice. These newer technics hold out promise of improved tumor control coupled with decreased normal tissue damage.

Intra-operative Radiation Therapy (IORT)

IORT is an investigational treatment used to treat cancers which by virtue of their location and pattern of spread are unlikely to be resectable for cure, and equally unlikely to be controlled by conventionally administered external beam radiation therapy (RT). It was introduced in Japan in the 1960s and began to be developed in the United States in the late 1970s. It is administered to the tumor or tumor bed during an operative procedure. IORT has been used in the management of several intra-abdominal malignancies including gastric, pancreatic, biliary, and rectal cancers. It has also been investigated in the treatment of retroperitoneal sarcomas, and carcinomas of the bladder.

In virtually all cases IORT has been used as part of a planned course of combined treatment which includes pre-operative RT and tumor resection. IORT is most often administered following resection of the primary tumor. A single, high dose of radiation is administered to the tumor bed usually in doses of 2000 to 3000 cGy. The intra-operative radiation beam must be able to deliver this dose of radiation to a limited depth, thus protecting underlying

tissues and organs from radiation injury. The electron beam is ideally suited for this, and in most cases electrons in the range of 10 to 15 MeV are used. In some institutions, orthovoltage X-rays have been utilized, thus producing a somewhat similar distribution of radiation. In those institutions in which IORT is available, either a dedicated operating room is equipped with a linear accelerator or more commonly, a radiation therapy room in the department of radiation oncology is converted to an operating suite. Often the resection is performed in the operating room, and the patient is then transported while under anesthesia to the radiation oncology department. IORT is then administered and the wound is closed.

Tepper et al have reported on their efforts to control locally advanced rectal cancer with the use of IORT.¹ Patients received high dose pre-operative RT to 5000 cGy followed by resection and IORT. Both primary and recurrent rectal cancers were treated. All patients were felt to have locally advanced tumors which would make curative resection unlikely. Most had tumor fixation to the pelvic sidewalls or sacrum. Eighty-seven patients were taken to surgery following pre-operative RT. Twelve did not receive IORT because metastases were found. Of the remaining 75, 58 received IORT. IORT was utilized in those patients in whom there was residual fixation of the rectum, or in those in whom there was residual tumor post resection. Of those with locally advanced primary tumors, the 3 year actuarial survival in those who received IORT was 58%. In those with recurrent rectal carcinomas, it was 32%. Local control rates ranged from 92% in primary tumors completely resected with IORT to 57% in recurrent tumors similarly treated.

These cases compare very favorably both in regard to survival and local control to series reported in the literature of patients who received pre-operative radiation only. It is felt that the excellent local control rate is a function of the higher radiation dose which can be administered using IORT as a supplement to external beam RT.

IORT has generally been well tolerated. Early studies failed to demonstrate an increase in severe complications as compared to patients treated with pre-operative radiation and surgery.² It is quite clear that single large doses of radiation can be administered directly to tumors or tumor beds without incurring excessive risk of radiation damage to normal structures.

Intra-operative radiation therapy . . . may have some promise in the management of advanced rectal cancer, and may have a role in selected pancreatic carcinoma.

At present IORT is still an appealing investigational tool. It appears to have some promise in the management of advanced rectal cancer, and may have a role in selected pancreatic carcinomas. Its usefulness in other intra-abdominal malignancies needs further evaluation. It is a complex technique requiring a large expenditure in resources and personnel. Its use at present should be restricted to those institutions conducting carefully designed clinical trials.

Altered Fractionation

The term "conventional fractionation" is used to describe the delivery of one 175 to 200 cGy dose of radiation per day in the treatment of malignant disease. Today, that concept is being questioned as investigators look for

altered fractionation schemes that may increase the therapeutic ratio between tumors and normal tissues.³

Repair of sublethal injury, regeneration, redistribution and reoxygenation have been described as the "4 Rs" of radiotherapy. There are 3 different tissue types that will behave differently to each of those processes: Early responding normal tissues (such as mucous membranes, hematopoietic tissue), late responding tissues (such as nerve tissue and dermis) and tumors, keeping in mind that tumors are very heterogeneous in their doubling times and ability to regenerate.

Repair of sublethal injury has been extensively studied and it is clear that the 3 types of tissues (early, late, tumor) have different capacities to repair injury. Historically, protraction of a course of radiotherapy and the use of small daily doses enabled the radiotherapist to give large total doses while protecting the patient from severe acute reactions. It is accepted that doses of 175 to 200 cGy per day, 5 days a week result in acceptable acute reactions. Therefore, the total dose will be determined by the late responding tissues which appear to have the capacity to repair sublethal injury more efficiently than the early responding tissues. The differential sparing of early and late reacting tissues as well as tumor cells is explained by the capacity of the surviving cells to regenerate. This is determined by the normal cell cycle time of the tissue and the dose rate and total dose that the tissues are exposed to. Altered fractionation is a deviation from standard fractionation to a regimen that will increase the therapeutic ratio by taking advantage of the differences in response to fractionation of normal tissues and tumor.

In accelerated fractionation, the overall treatment time is shorter than with conventional fractionation by using 2 or 3 doses per day. The total dose and fraction size remain similar to conventional fractionation. In rapidly proliferating tumors, a gain in local control should result if one administers radiation therapy in a shorter overall time, thereby reducing the opportunity for tumor cell proliferation.

In hyperfractionation, the fractional doses are smaller and are delivered 2 or 3 times per day allowing for an increase in the total dose but given over the same overall time as conventional fractionation. One can also combine principles of accelerated fractionation and hyperfractionation and use a plan where the fraction size is lower, the number of fractions is higher and the overall treatment time is decreased compared to standard fractionation.

The first data reporting the use of accelerated fractionation was for the treatment of glioblastoma multiforme, in which there was no improvement in survival rate when compared to standard fractionation. This may have been related to the low doses used. Another study looked at accelerated fractionation in the treatment of Burkitt's lymphoma.⁴ In those patients treated with once a day fractionation using a daily dose of 220 cGy for a total of 3100 cGy over 20 days, only 1 out of 9 patients achieved a complete response. Nevertheless, in patients treated to total dose of 2900 cGy in 27 fractions over 13 days using twice-a-day radiation therapy, 25 out of 34 achieved a complete response.

The most studied tumors using altered fractionation schemes have been squamous cell carcinomas of the upper aerodigestive tract. C. C. Wang of Massachusetts General Hospital and Rod-

ney Million at the University of Florida, Gainesville, have published extensively on this topic.

Early stage head and neck tumors tend to have good 3 year disease-free survivals using conventional fractionation but unfortunately, local control is much more difficult with stage III and IV lesions. Much of the research in twice-a-day (bid) radiation therapy in head and neck cancer has been directed at optimizing disease-free survival in these groups of patients. Wang has utilized a regimen of bid fractionation for T₃ and T₄ supraglottic carcinomas.⁵ Patients receive 160 cGy per fraction, 2 fractions per day, 5 days per week to 6400 cGy with a 2-week rest after the second week of therapy. When compared to patients receiving standard once-a-day fractionation of 180 cGy to a total dose of 6500 cGy there was an increase in local control from 50% to 76% with twice-a-day radiotherapy. Wang has also demonstrated similar results at other head and neck sites.⁶ This technique consisting of a 2-week break in treatment has been criticized by some who believe that the interruption may allow for tumor cell repopulation.

Million et al have also published extensively on this topic.⁷ Stage III and IV squamous cell carcinomas of the head and neck are treated with a twice-a-day radiation consisting of 120 cGy per fraction with a 4 to 6 hour interval between doses to total doses of 7440 to 7920 cGy. When compared to historical controls treated with once-a-day radiotherapy there was an improvement in local control of greater than 10 to 15%. Because of the lower dose per fraction, this regimen is tolerated without planned treatment breaks and it is possible to escalate the total dose.

The Radiation Therapy Oncology Group (RTOG) has con-

ducted studies to determine the dose fraction that would permit bid treatments without the need for a rest.⁸ They reported that doses of 150 cGy bid still resulted in such severe acute reactions that a rest period was needed. Doses in the range of 125 cGy were better tolerated. A phase III RTOG study of hyperfractionated radiotherapy was then conducted but low total doses were utilized and no significant difference was found between the regimen and standard fractionation.⁹ Since then, a number of RTOG trials have been conducted searching for the optimal total dose for local control. The preliminary results of RTOG Protocol 83-13 were recently published.¹⁰ Twice-a-day radiation therapy was delivered using 120 cGy fractions to total doses of between 6720 cGy and 8160 cGy. Higher local control rates with 7200 and 7680 cGy suggested an improved outcome. A phase III study is underway to compare hyperfractionated radiotherapy with 120 cGy bid with standard fractionated doses.

Radiobiologically altered fractionation is advantageous in selected cases; nevertheless, there are other factors that need to be considered. The emotional, physical and financial strain on the patient and family can be significant. Not only is the treatment physically demanding, but the logistics of twice or thrice-a-day transportation to a radiation therapy facility may be prohibitive. In addition, in an era of radiation technologist shortage, it is extremely difficult for many radiation therapy facilities to employ this mode of treatment on large numbers of patients.

Computer Assisted Treatment Planning and Dosimetry

Radiation treatment planning is a broad-based term given to the process of evaluating a patient's

detectable and potential tumor extent, choosing an appropriate modality (photons, electrons, teletherapy, brachytherapy) and applying that modality in the optimum arrangement and technique to maximize the tumor dose while minimizing the normal tissue dose. Dosimetry is the process of calculating the dose distribution provided by the treatment planning parameters. In the last 15 years, several new technologies have dramatically added to the available solutions. Foremost among these are the new imaging techniques of computerized tomography (CT) and magnetic resonance imaging (MRI). A second area of technologic advance is the development of increasingly inexpensive and more powerful mini and micro-computer systems dedicated to radiation treatment planning and dosimetry.

Computerized tomography has revolutionized the planning of treatment, both because it can often detect the presence and define the extent of a soft tissue mass which could not otherwise have been seen, and because it has permitted the confident localization of uninvolved organs which one would like to spare from the consequences of irradiation.¹¹ The application of MRI to treatment planning and dosimetry has not yet matured to the point where its impact can be assessed, but, like CT, it will soon become an integral part of the imaging armamentarium available to the radiation oncologist.

In the early 1970s, when CT and first generation treatment planning computers became available to a fortunate few institutions, analysis was limited to two-dimensional considerations. The computer could only consider one or, at best a few, transverse sections through the patient and required that the radiation beams be parallel to those sections. Such

limitations have some serious defects. First, the physician may be lulled into a false sense of security in a plan which appears satisfactory in the section studied, but may have serious under or over-dosed areas in other unexplored parts of the treatment volume where the contour may differ, or the relationships between tumor and normal tissues may change. In addition, by limiting the choices to co-planar beams, one is prevented from trying the most sophisticated, customized approach to optimizing therapy.

Now that computing power has increased, and computer cost has decreased, we are beginning to see true 3 dimensional systems which are available to any size facility. The computer can now quickly and interactively provide the physician with a "beams eye view," allowing almost infinite adjustment of beams in all 3 axes so that sensitive normal structures like the spinal cord, kidney or lens can be spared excessive dosage. Multi-beam or rotational techniques, which used to take from 10 to over 60 minutes to calculate, are now ready in seconds. In the past, the physician might be inclined to accept the initial plan in the interest of expediency and throughput; now he or she has the luxury of evaluating multiple plans in search of the optimum beam arrangement.

Stereotactic Radiosurgery

In most clinical settings, radiation therapy must be carefully planned to encompass not only the entirety of the primary tumor, but also the known and unknown lymphatic extensions of the tumor. This unavoidably entails covering a volume of normal tissues in the treatment region. All possible techniques to limit the amount of normal tissue dosage are then brought into play. In some "lucky" settings, however,

the lesion to be treated is small, well localizable and has essentially no capacity to have unsuspected regional extensions. For the most part, this situation obtains for intracranial neoplasms and arteriovenous malformations (AVMs). Conceptually, one could use extremely high radiation doses by meticulously planning the therapy to sharply avoid any substantial amount of normal brain tissue. The high radiation dose to the lesion should result in an enhanced control rate, while the low dose to the surrounding tissues should minimize early and late (ie permanent) toxicity.

Radiosurgery actually began in the early 1950s when Lars Leksell, a Swedish neurosurgeon, modified his stereotaxic surgical frame to accept a narrowly collimated orthovoltage X-ray beam.¹² In addition to treating small tumors and AVMs, Leksell and his colleagues also used the technique to create therapeutic areas of necrosis (so called thalamotomies) for relief of intractable pain. Based on his early success, Leksell sought to improve the penetration and distribution of his radiation dosage, as well as to minimize the time and number of beams necessary. His solution was to use a charged particle beam, which exhibits a phenomenon known as a Bragg peak. The beam will pass through tissue without depositing much energy until it reaches a finite depth (determined by its energy) where it will sharply give up all its energy and essentially stop. The proton beam from a cyclotron was chosen as the modality. With this technique, many patients were successfully treated for AVMs, pituitary adenomas and hyperpituitarism. The technique was adapted in this country by Kjellberg et al and Fabrikant et al.^{13,14} With Bragg peak therapy, single doses of from 2000 to 18,000 cGy can be safely and ef-

fectively administered.

Another technique, which was also pioneered by Leksell, is the "Gamma Knife" technique, using multiple Cobalt 60 sources geometrically arranged to produce pencil beams aimed at the target of interest. The prototype unit contained 179 individual 1mm diameter sources. Subsequent "production units" have been fashioned with 201 separate sources, thus increasing the dose rate. In this country, most of the experience has come from the Presbyterian University Hospital of Pittsburgh, which has been operating their unit since August of 1987. Patients are admitted to the hospital the day before treatment. The next morning, the patient is brought to the gamma knife suite. After local anesthesia and intravenous sedation, the stereotactic frame is attached by 4 pins drilled into the outer surface of the patient's skull. Once fixed, the frame remains in place until the treatment is completed. The patient is then brought to the Radiology department for imaging. This may take the form of CT scanning, magnetic resonance imaging, cerebral angiography or orthogonal x-rays. The patient is brought back to the treatment suite and waits while the X, Y and Z coordinates of the target area are chosen and computerized dosimetry is performed. The patient is then "docked" with the gamma knife unit itself, and after precise positioning, the treatment is given. Depending on the dose required, the treatment may take from one to several hours. Fewer than 20% of the patients experience mild headache, nausea or vomiting. Of the 210 patients treated in Pittsburgh, 96% were discharged within 24 hours of treatment.¹⁵ Some degree of field shaping is possible by plugging some of the 201 source apertures, so that, for instance, the optic chiasm can be

shielded while delivering a high dose to the pituitary gland.

The latest technique for doing radiosurgery involves the use of a linear accelerator as the source of radiation. These units are variously referred to as the "X-ray knife," "photon blade" or "linac scalpel." The first radiosurgically modified linear accelerator in this country was established at the Brigham and Women's Hospital in 1986. Since that time, approximately 40 other centers have started similar programs. The accelerators are modified to produce pencil beams from 12 to 30mm in diameter. The beam is delivered in a series of non-coplanar 180 degree arc rotations. At some centers, a computer controls the motions, and may also rotate the treatment couch dynamically during radiation to further refine (and confine) the dose distribution. The main advantage of the linear accelerator based units are the increased dose rate, and the lack of need of replacing multiple cobalt sources as they decay in activity.

As noted above, radiosurgery has been used for a variety of malignant as well as non-malignant disease. Early results have been mixed. Most groups reporting on AVM treatment show a 60 to 90% complete response rate with a low incidence of serious toxicity. The results with acoustic neuromas indicate an 85% control rate, but a 25% incidence of facial weakness and a 60% incidence of hearing deterioration. For pituitary adenomas, one can find evidence for an 85 to 90% long term control rate, with a 10 to 15% incidence of hypopituitarism. Other lesions being treated by radiosurgery include astrocytomas, glioblastomas, metastatic lesions, meningiomas, craniopharyngiomas, pinealomas, ependymomas, medulloblastomas and hemangioblastomas. In addition,

some groups are investigating radiosurgery as an adjunct to conventional RT. There are no reported series yet for these entities from which to draw any meaningful conclusions.

Brachytherapy

Brachytherapy is carried out by placing radioactive sources within or at the immediate vicinity of a tumor. The following techniques are available to achieve this placement: intraluminal, interstitial, intracavitary, or surface-mould. Modern era brachytherapy began in the 1950s when Henschke in the US and Pierquin and Chassagne in France introduced the afterloading technique.^{16, 17} The advent of computers has allowed comprehensive display of the dose distribution surrounding radioactive implants. Currently a resurgence of interest is occurring because of technological developments in radioactive nuclides, instrumentation, and remote-afterloading devices.

Radium as the implant source was used almost exclusively in the first half of this century. The continuing proliferation of man-made radioactive nuclides of different source energies, such as iridium-192, cesium-137, iodine-125, and palladium-103 has allowed easier shielding and protection. Technological improvements have provided miniaturization of radioactive sources, as well as sources with high specific activity. Progress in the plastics and electronics industries gave birth to sophisticated treatment applicators and remote-afterloading devices that allow accurate mobilization of sources from a protected storage safe via flexible transit tubes to the treatment applicator by remote control. The concept of afterloading the radiation sources into rigid or non-rigid guide systems, that have been carefully im-

planted according to a pre-planned pattern, greatly reduced radiation exposure while achieving precision in the implantation.

Traditional brachytherapy is different from external beam therapy in that the irradiation is given continuously at a low dose rate over several days. The radiobiological effect is different. The lesions treated are usually selected by their anatomical accessibility and relative small size. The physical dose distribution is very different from external beam irradiation because dosage is localized to the target volume with rapid fall-off in adjacent normal tissues. Recently, high dose rate radiation sources have been utilized in brachytherapy. The high specific activity of iridium-192 allowed production of the sources in very small dimensions, and its relative low energy gamma emissions limit the dose penetration to adjacent normal tissues. High dose rate brachytherapy expanded the utility of this modality into more anatomical sites, such as bronchus, brain and esophagus. Combined with the sophistication of computerized afterloading systems, these sources can be withdrawn incrementally through an applicator and dwell for a given period of time in each stop position to create an optimized dose distribution.

As curative treatment, brachytherapy has given good results in select, early, radiocurable cancers. In the head and neck area, many upper aerodigestive tumors are accessible to direct instrumentation, such as the lips, oral cavity, buccal mucosa, oral tongue, and floor of mouth. The cure rates of 70%-90% for early lesions compare favorably with surgery or external beam therapy.¹⁶ The advantage over external beam therapy is the sparing of salivary tissues and other cervicofacial tissues. It is ideal as a

supplemental treatment boost to external beam therapy in order to take a smaller volume to a high dose. It is also an alternative to surgery or chemotherapy for locally recurrent tumors or new primaries in previously irradiated areas. Recurrent nasopharyngeal cancer is very effectively treated by this method. In gynecological tumors, the results of cesium-137 and iridium-192 as substitutes for radium-226 have maintained the excellent results long established.^{17, 18} Early lesions of the bladder, penis, and prostate have been treated with success rates comparable to surgical treatment.¹⁹⁻²¹ For tumors of the anorectal regions, select early lesions yield tumor control rates of 70%-80%.²² In the management of breast cancer, breast preservation for small (T-1, T-2) primary tumors can be achieved with good cosmesis through the combination of external beam therapy and brachytherapy as treatment boost.²³

Many tumors are now treated palliatively by brachytherapy in areas such as the brain, esophagus, bronchus, pancreas and bile ducts.

Many tumors are now treated palliatively by brachytherapy in areas such as the brain, esophagus, bronchus, pancreas and bile ducts. In general, they provide short duration of symptom relief.

Future developments are aimed at defining the role of brachytherapy in current cancer treatment by exploring its application for the various types of tumors at different anatomical sites. Towards this goal clinical trials are conducted to evaluate brachytherapy used alone or in combination with other modalities, such as hyperthermia and chemotherapy.^{24, 25}

Hyperthermia

The effect of heat on malignant tumors was first appreciated by Hippocrates. In the nineteenth century, this phenomenon was rediscovered by Busch who described the spontaneous disappearance of a soft tissue sarcoma following a high fever in a patient with erysipelas.²⁷ Subsequent attempts at inducing fevers in cancer patients with pyrogenic toxins demonstrated some marginal responses.

In the early 1900s, the development of radiofrequency generators stimulated some initial enthusiasm for localized hyperthermia treatment; however this was short-lived. Over the last two decades, renewed interest in this modality followed a number of systematic laboratory investigations which demonstrated that hyperthermia, either alone or in conjunction with radiation therapy or chemotherapy, could enhance the killing of tumor cells. These studies continue to support the use of hyperthermia in cancer therapy.

There are a number of complex interactions that occur when heat is combined with radiation therapy. The net effect of these changes has been a thermal enhancement of radiation sensitivity. The sensitizing effect of heat given in conjunction with radiation is due to two different factors. The first is that hyperthermia has been shown to inhibit repair of radiation damage.²⁸ The second is that two types of cells that are relatively radiation resistant (hypoxic cells and S phase cells) have been found to be particularly heat sensitive. The fact that human tumors frequently contain hypoxic regions as well as cells dispersed throughout all phases of the cell cycle supplies the theoretical rationale for employing these complementary modalities in hopes of enhancing cellular cy-

totoxicity.

Numerous clinical studies have reported on the efficacy of hyperthermia given alone or in conjunction with radiotherapy. The majority of these reports have involved the treatment of superficial tumors because of their relative accessibility for heating when compared to more deeply seated tumors. In a recently updated review, Overgaard found surprisingly consistent results when looking at response rates in collected series of patients with superficial tumors. This was true even though radiation dose and fractionation as well as hyperthermia techniques varied greatly from study to study. Complete response rates for patients treated with hyperthermia alone were about 15%, with radiotherapy alone about 35%, and with combined radiotherapy and hyperthermia approximately 70%. Treatment related toxicity consisted primarily of thermal burns and occurred in about 15% of patients.^{30, 31} In another more recent study, Steeves did a matched-pair analysis of multiple lesions in patients where one lesion received radiation alone while the other received radiation plus hyperthermia. In this series, combined modality treatment demonstrated a statistically significant improvement in response rate (45% vs 30%).³⁴

Perez et al have reported their results using combined hyperthermia and radiotherapy for locally recurrent chest wall disease in breast cancer. Although this non-randomized trial is limited by its use of historic, radiation only controls, its positive results are still encouraging. In this study, smaller chest wall lesions had a marked improvement in complete response rates when hyperthermia was given in conjunction with radiotherapy versus radiotherapy alone (80% vs 33%).

In addition, an analysis of tumor control rates (defined as freedom from disease progression for more than 6 months following completion of treatment) also revealed improvement for those receiving combined modality treatment.³³

Another disease site where hyperthermia has been studied is in the management of metastatic melanoma. Kim et al treated more than 100 metastatic melanoma lesions in 38 patients with radiotherapy alone or in conjunction with hyperthermia. Once again the overall tumor control rate of the combined therapy group was superior to radiotherapy alone (75% vs 46%). In addition, normal tissue toxicity was comparable between the two groups.²⁹ Although survival was not evaluated in this study, there is data which suggest that patients with recurrent melanoma who achieve local control at the site of initial metastasis may have an actual survival advantage over those who do not.³²

... a combined hyperthermia/radiotherapy approach continues to show promise in improving tumor response and local control in cancer patients for whom conventional therapy offers low efficacy.

A third site where a combined hyperthermia/radiotherapy approach has been extensively studied and shows promise is in the management of neck node metastases from squamous carcinomas. In one recent series, 38 patients with a total of 81 multiple neck node metastases were treated with either radiotherapy alone or in conjunction with hyperthermia.²⁶ Patients had one of their neck nodes treated with hyperthermia and radiation and the remaining nodes treated with ra-

diotherapy alone. Complete response rates in this series were 79% for lesions treated with combined therapy versus 42% for those treated with radiotherapy alone. At two years following treatment, local tumor control was also significantly improved in the combined treatment group.

Recent technical advances in heat delivery allow greater accessibility to more deeply seated lesions. Current investigations are underway to study the potential role of hyperthermia at a number of different sites including advanced pelvic tumors, unresectable sarcomas, and CNS neoplasms.

Both laboratory and clinical work support a role for hyperthermia in cancer therapy. At this time, a combined hyperthermia/radiotherapy approach continues to show promise in improving tumor response and local control in cancer patients for whom conventional therapy offers low efficacy. Current research efforts are aimed at further elucidating the mechanisms of hyperthermic cell kill as well as improving the technology of its application. Novel approaches such as interstitial thermoradiotherapy and trimodality therapy (hyperthermia, radiotherapy, and chemotherapy) are other avenues of active hyperthermia research.

Conclusion

We are experiencing an exciting period in radiation oncology with respect to the potential for improvement in the therapeutic ratio made possible by the new techniques and technologies presented in this article. It is too early to say what the impact of these new advances will be on the outcome of treatment, but it is hard to imagine that it will not be both beneficial and substantial. Morbidity of therapy should certainly be reduced. It is likely, too, that

tumor control, and hence long term survival, will be improved both through more complete tumor coverage and, by taking advantage of the improved ability to spare normal tissues, by allowing more aggressive tumor therapy.

What do the 1990s hold for further improvement in the efficacy of radiation therapy? Work is already underway on refining combined modalities of treatment (biological response modifiers, combinations of chemotherapy and radiation, "magic bullet" type systemic radiation through radioactively tagged tumor immune complexes). In addition, we can expect more precise delivery of radiation through more sophisticated computer control, including real-time monitoring and feedback loop adjustment of daily treatment by remote, or even in-situ detectors.

While we wait for our basic science colleagues to unlock the ultimate molecular secrets of the various diseases we call cancer, and provide the genetic tools or vaccines to prevent them, we are faced with one million new cancer patients each year who must be offered the best possible chance for cure. Hopefully, we have taken a meaningful step in that direction with the advances presented here.

References

1. Tepper JE, Wood WC, and Cohen AM: Treatment of Locally Advanced Rectal Cancer with External Beam Radiation, Surgical Resection, and Intra-Operative Radiation Therapy. *Int. J. Radiation Oncology Biol. Phys.*; 16:1437-1444. June 1989.
2. Tepper Joel E, Gunderson Leonard L, Orloff Erica, Cohen Alfred M, Hedberg Stephen E, Shipley William U, Blitzer Peter H, Rich Tyvin: Complications of Intraoperative Radiation Therapy: *Int J Radiation Oncology Biol Phys* 10:1831-1839. October 1984.
3. Withers HR, Biologic Basis for Altered Fractionation Schemes. *Cancer* 1985;55:2086-2095.
4. Torsten N & Onyango Julius. Radiotherapy in Burkitt's Lymphoma. Conventional or Superfractionated Regime — Early Results. *Int. J. Radiation Oncology Biol. Phys* 1977;2:399-406.

- Wang CC et. al. Twice-a-Day Radiation Therapy for Supraglottic Carcinoma. *Int. J. Radiation Oncology Biol. Phys.*; 1986;12:3-7.
- Wang CC et. al. Twice-a-Day Radiation Therapy for Cancer of the Head and Neck. *Int. J. Radiation Oncology Biol. Phys.*; 1985;55:2100-2104.
- Parsons JT et. al. Hyperfractionation for Head and Neck Cancer. *Int. J. Radiation Oncology Biol. Phys.*; 1988;14:649-658.
- Marks R et. al. Hyperfractionation — Where We Stand — A Preliminary RTOG Report. *Proc. Am. Soc. Ther. Radiol.* 4:139-140; 1978.
- Marcial VA et. al. Hyperfractionated Photon Radiation Therapy in the Treatment of Advanced Squamous Cell Carcinoma of the Oral Cavity, Pharynx, Larynx & Sinuses, Using Radiation Therapy as the Only Planned Modality: (preliminary report) by the Radiation Therapy Oncology Group. *Int. J. Radiation Oncology Biol. Phys.* 13:41-47; 1987.
- Cox J et. al. Dose-Response for Local Control with Hyperfractionated Radiation Therapy in Advanced Carcinomas of the Upper Aerodigestive Tracts: Preliminary Report of Radiation Therapy Oncology Group Protocol 83-13. *Int. J. Radiat. Oncol. Biol. Phys.*, 18:515-521; 1990.
- Goitein M, et. al., Applications of computed tomography in radiotherapy treatment planning. In: Orton, C., ed. *Progress in Medical Radiation Physics*, vol. 1. New York: Plenum Press, 1982;195-293.
- Leskell L.: The Stereotactic Method and Radiosurgery of the Brain. *Acta Chir Scand* 102:316-319, 1951.
- Fabrikant et. al.: Stereotactic Heavy-Ion Bragg Peak Radiosurgery for Intra-Cranial Vascular Disorders. *Br. J. Radiol.* 57:479-490, 1984.
- Kjellberg et. al.: Bragg Peak Proton Beam Therapy for Arteriovenous Malformations of the Brain. *N. Engl. J. Med.* 309:269-274, 1983.
- Wu et. al.: Physics of Gamma Knife Approach on Convergent Beams in Stereotactic Radiosurgery. *Int. J. Rad. Onc. Biol. Phys.* 18:941-949, 1990.
- Pierquin B, Wilson JF, & Chassagne D: *Modern Brachytherapy*, Mason Publishing USA. New York, 1987.
- Henschke UK: Afterloading Application for Radiation Therapy of Carcinoma of the Uterus. *Radiology.* 74:834, 1960.
- FIGO: Annual Report on Results of Treatment in Gynecological Cancer. Pettersson, F. (Ed) Vol 20, Radiumhemmet, Stockholm, 1988.
- van der Werf-Messing BHP, Menon RS, & Hop WCJ: Cancer of the urinary bladder category T2, T3, (N₀M₀) treated by interstitial radium implant: second report, *Int. J. Radiation Oncology Biology & Physics*, 9,481-485, 1983.
- Mazeron JJ, Langlois D, Lobo PA, Huat JA, Calitchi E, Lusinchi A, Raynal M, Le Bourgeois JP, Abbou CC, Pierquin B: Interstitial radiation therapy for carcinoma of the penis using Iridium 192 wires: The Henri-Mondor Experience (1970-1979). *Int. J. Rad. Onc. Biol. Phys.*, 10, 1891-1895, 1984.
- Whitmore WF, Hilaris BS, Sogans PC, Herr HW & Fair WR: Interstitial irradiation with iodine-125, management of clinically localized prostate cancer, NIH Consensus Development Conference, 36-37, National Institutes of Health: Bethesda, 1987.
- Papillon J: *Rectal and Anal Cancers*, Springer-Verlag. Berlin-Heidelberg-New York, 1982.
- Leung S, Otmertzguine Y, Calitchi E, Mazeron JJ, Le Bourgeois, J. P. & Pierquin, B.: Locoregional recurrences following radical external beam irradiation and interstitial implantation of operable breast cancer: a 23 year experience, *Radiation & Oncology*, 5, 1-10, 1986.
- Wilson JF, Chassagne D & Joslin CAF: *Brachytherapy Trials*. *Int. J. Radiation Oncology Biology and Physics.* 14, Supplement 1:557, 1988.
- Emami B & Perez C: Interstitial Thermo-Radiotherapy: An Overview. *Endocurietherapy Hyperthermia.* *Oncology* 1:35, 1985.
- Arcangeli G, Arcangeli GC, Guerra A, et. al.: Tumor response to heat and radiation: Prognostic variables in the treatment of neck node metastases from head and neck cancer. *Int. J. Hyperthermia* 1:207-217, 1985.
- Busch W: Über den Einfluss Weichen heftigere Erysipelen zuweilen auf Organsierte Neubildungen Amiben. *Verh des Naturh: Preuss Rheinl.* 23:28, 1866.
- Henle KJ, Leeper DB: The modification of radiation damage in CHO cells by hyperthermia at 40 and 45 degrees centigrade. *Radiation Research* 70:415-424, 1977.
- Kim JH, Hahn EW, Ahmed SA: Combination hyperthermia and radiation therapy for malignant melanoma. *Cancer* 50:478-482, 1982.
- Oleson Jr: Hyperthermia. In DeVita VT, Hellman S, Rosenberg SA (eds): *Cancer, Principles and Practice of Oncology*, 3rd ed., 2426-2435, 1989.
- Overgaard J: Rationale and problems in the design of clinical studies. In Overgaard J (ed): *Hyperthermic Oncology*. London, Taylor & Francis, vol. 2, pp 325-338, 1984.
- Overgaard J: The role of radiotherapy in recurrent and metastatic melanomas: A clinical radiobiological study. *Int. J. Radiat. Oncol. Biol. Phys.* 12:867-872, 1986.
- Perez CA, Kuske RR, Emami B, Fineberg B: Irradiation alone or combined with hyperthermia in the treatment of recurrent carcinoma of the breast in the chest wall: A non-randomized comparison. *Int. J. Hyperthermia* 2:179-188, 1986.
- Steeves RA, Severson SB, Paliwal BR, Anderson J, Robins HI: Matched pair analysis of response to local hyperthermia and megavoltage radiation therapy for superficial human tumors. *Endocurietherapy/Hyperthermia Oncology* 2:163-170, 1986.

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1. Data on file, G.D. Searle & Co.
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BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration.

Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°, 2°, 3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomastia, increased urination, spotty menstruation, impotence.

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SEARLE

Post-Mastectomy Reconstruction of the Breast Utilizing the Transverse Rectus Abdominis Myocutaneous Flap

Armand D. Versaci, MD

... there are still many patients who are not suitable candidates for the operations that rely on the use of alloplastic materials.

Introduction

During the past 10 years we have seen an enormous growth in interest for post-mastectomy breast reconstruction. This phenomenon has been fueled by the introduction of the tissue expander which is used to provide skin coverage for a silastic breast-shaped prosthesis.^{1,2} The expander is placed beneath the skin and muscles of the lower thoracic region, and then slowly inflated with saline. After a skin mound of appropriate size develops, a silastic prosthesis is exchanged for the expander thereby creating a breast reconstruction.

The latissimus dorsi myocutaneous flap was re-discovered just prior to this time.^{3,5} For a period of time it was considered to be the ideal way to reconstruct the breast. Although it was utilized successfully by many surgeons,

there were others who felt that there were definite deficiencies in the quality of the reconstructions achieved. In 1979 Robbins and in 1982 Hartrampf reported on their studies and successes in the use of the lower abdominal skin and fat, which is carried on the rectus abdominis muscle pedicle, for the reconstruction of the breast.^{6,7} This has become known as the TRAM flap (transverse rectus abdominis myocutaneous flap) method of breast reconstruction.

Since the transverse rectus abdominis myocutaneous flap was first developed, it was recognized as having the potential for superseding the then popular latissimus dorsi myocutaneous flap method of breast reconstruction. In fact, it has become the benchmark for measuring the quality of every method that relies on the use of autologous tissues in the reconstruction.

We have been using the method and find that, although it is a major surgical procedure, the quality of the reconstruction achieved, in a select group of patients, warrants that we continue its use when we are convinced that one of the simpler methods will not be as good.

The simpler methods rely on the use of a silastic breast prosthesis to create the breast mound.⁸⁻¹¹ It is the most commonly used method of breast reconstruction. Its applicability has been enhanced by the introduction of the tissue expander. Although its use has extended the indications for the use of breast prostheses, there are still many patients who are not suitable candidates for the operations that rely on the use of alloplastic materials. This latter group of patients form the basis for this report on the use of the TRAM flap method of breast reconstruction. The author has performed 26 TRAM flap breast reconstructions over the past several years. Most were performed during the past 2 years.

Patient Selection

Some patients refuse to consider reconstruction if the reconstruction involves the use of a silastic implant. They are aware of the TRAM flap method of reconstruction and often request it (figure 1). The TRAM method is indi-

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ABBREVIATIONS USED:

TRAM flap: transverse rectus abdominis myocutaneous flap

cated when a radical mastectomy has been performed, or when the pectoral muscles have been denervated during the performance of a modified radical mastectomy. Radiation damage of the skin also precludes the use of alloplastic materials but not the TRAM flap which derives its blood supply from the rectus abdominis muscle (superior epigastric vessels). Previous failures with other methods is another indication, as is the presence of a large opposite breast which cannot be easily matched by any other method of reconstruction. The use of the method is predicated on the presence of a favorable abdomen that is free of scarring in the critical area of blood supply to the muscle and the proposed skin flap. The final consideration is the health status of the patient that will allow for the operation to be safely undertaken. Obesity is one of the important health considerations since the incidence of complications does rise in overweight patients.

Surgical Technique

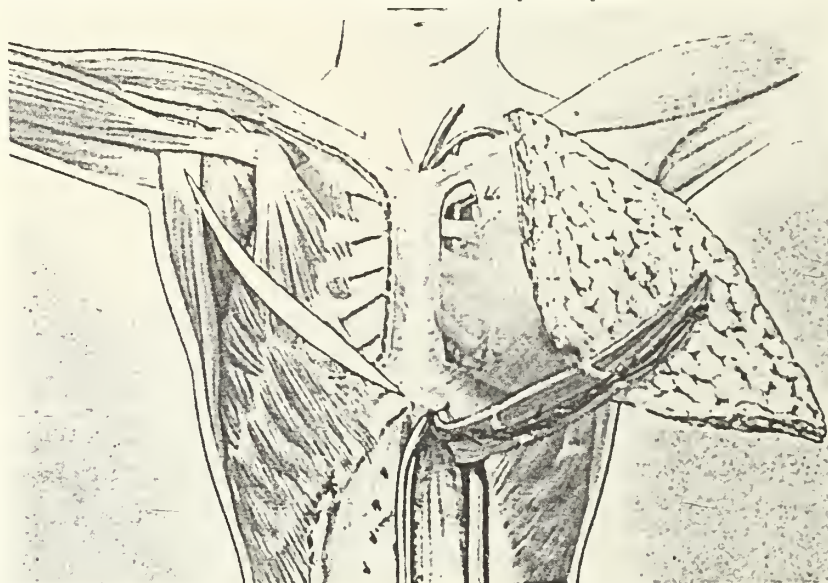
In brief, a transversely oriented flap of skin and fat is designed and raised, but it is left attached to one of the rectus abdominis muscles with its overlying anterior rectus sheath (figure 2). The donor muscle is divided along with the inferior epigastric vessels just above the inguinal area. The muscle is then freed from its bed along with the anterior rectus fascia. The entire unit is freed upwards to the level of the costal margin. A subcutaneous tunnel is created above this point toward the area of the proposed breast reconstruction (figure 3). The skin flap along with the muscle is passed through the tunnel where it will ultimately become the breast mound. The breast is reconstructed by tailoring the available tissue into the new breast

Figure 1. Patient Selection

PATIENT SELECTION

- **Patient's desire**
- **Radical mastectomy**
- **Radiation damage**
- **Absent or denervated pectoralis muscle**
- **Large breast**
- **Previous failures with other methods**
- **Favorable abdomen and health status**

Figure 2. The left rectus abdominis muscle has been sectioned at its caudal margin. The inferior epigastric vessels have been divided. The muscle, along with the transverse abdominal flap, has been elevated out of its bed. The circulation of the unit is supplied by the superior epigastric artery which is the terminal branch of the internal mammary artery.



shape and then suturing it in place. The modeling must be done artistically if a pleasing shape is to be achieved.

Complications

The incidence of complications increases in patients who are moderately obese, and is found to be greatest in patients who are very obese.¹² The presence of obesity therefore becomes one of the important factors in selecting patients for the TRAM operation (figure 4).

The dreaded complication is the loss of viability of the transposed flap due to the failure of maintaining the patency of the vascular pedicle. This may be due to one of two factors. A misjudgment may occur in recognizing the area of skin and fat that is sufficiently vascularized to withstand transfer. Areas of tissue with marginal circulation may appear appropriately vascularized prior to transfer, but in fact cannot withstand the trauma of transposition. Experience has shown that

one should err on the conservative side when assessing tissue viability.

Radiation damage to the skin also precludes the use of alloplastic materials but not the TRAM flap which derives its blood supply from the rectus abdominis muscle . . .

The second misjudgment occurs at the time of transfer when inadequate length of the muscular pedicle, twisting of the pedicle, or tension across the pedicle may lead to flap necrosis. Today some surgeons use two pedicles to insure that the circulation to the flap is adequate. Other surgeons double the circulation to the transposed flap by doing microvascular anastomoses between the divided inferior epigastric vessels and vessels within the axilla. Our preference is to use only one pedicle, and to limit the amount of skin flap being harvested on the side of the abdomen opposite to the muscle flap being used.

The third complication is the development of an incisional hernia through the repaired rectus fascia that overlies the rectus abdominis muscle.

To date we have had partial losses of the distal end of two flap transfers. They were due to the transposition of tissue whose distal margin was in an area of questionable circulation. The first loss of tissue was small, so it was possible to modify the inset of the pedicle flap. The loss did not significantly detract from the quality of the reconstruction. The second was larger in size. The granulating wound was healed by applying a skin graft, and subsequently removing it when the inset was modified.

The third loss was more extensive. It was due to the twisting of

Figure 3. The flap is shown being transposed to the thoracic region through a subcutaneous tunnel. Once transposed, the donor area is sutured and the flap is then fashioned into a breast mound.

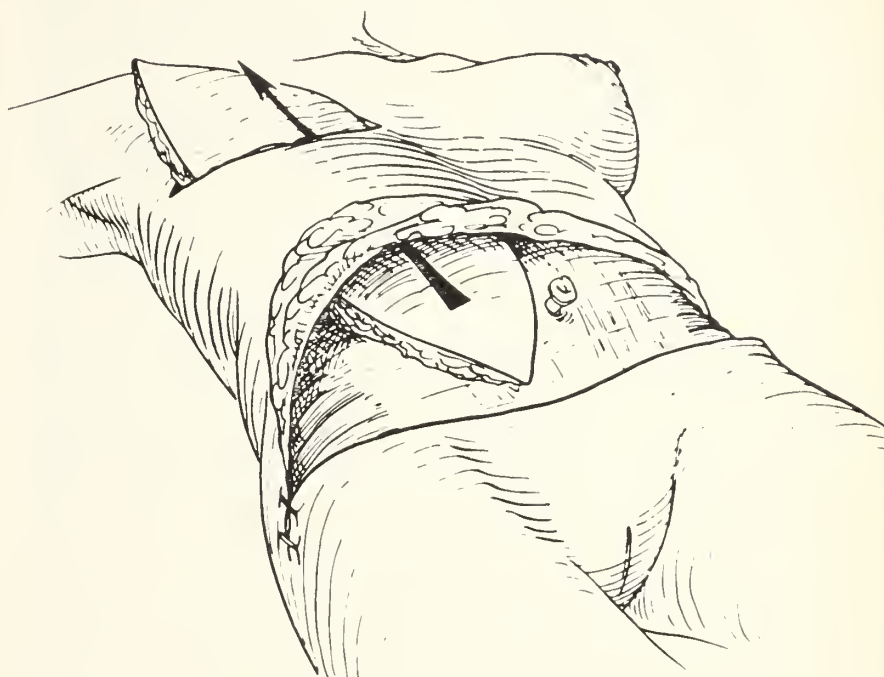


Figure 4. Major Complications

MAJOR COMPLICATIONS	Cases 26
• Flap necrosis	
Minor	2
Major	1
• Incisional hernia	1
• Phlebitis	0

the pedicle which occurred at the time that the musculocutaneous flap was transferred. The diminution in the circulation that resulted was not appreciated at the time of surgery. Loss of the distal one-half of the flap resulted. The reconstruction was salvaged by adding a breast implant beneath the segment of the transposed flap that survived. The secondary procedure was carried out after the wound had healed.

A ventral hernia developed in one patient. The abdominal

wound was explored, and a separation had occurred in a limited section of the sutured rectus fascia. This was repaired by identifying the two sides of the rectus sheath and the medial edge of the external oblique fascia. A two layer closure was utilized and it resulted in a successful repair. The two edges of the rectus fascia were sutured together. The repair was reinforced by advancing the fascia of the external oblique muscle and suturing it over the first layer of the repair.

Discussion

Patient selection is the most important factor when contemplating TRAM flap reconstructive surgery of the breast. Since there are many methods of reconstruction available, broad experience in the use of all available methods of reconstruction are critical in the selection process. One method may be clearly superior in a specific situation. In other situations, more than one method may be used with the expectation that an acceptable reconstruction will result. In certain select cases, the TRAM method is the only one which will satisfy the tissue needs of the reconstruction and still be done with an acceptable surgical risk.

The transposition of the flap as an initial event is the beginning of the reconstructive process. In the ideal situation, the only other stage is that of reconstructing the nipple-areola complex if the patient desires it.^{13, 14} This can be done by employing a variety of surgical techniques. In other cases, some additional procedure must be done at the time of the nipple-areola reconstruction in order to improve upon the quality of the reconstruction. This includes fine tuning of the mound, or surgery to achieve symmetry by performing an augmentation, mastopexy or reduction mammoplasty on the remaining breast.

One patient, whose remaining breast was quite large but whose abdominal wall was thin, desired the TRAM method of reconstruction but did not desire a reduction mammoplasty done on the remaining breast. The reconstruction achieved was not large enough to produce a breast which was equivalent in size of the remaining breast. Symmetry was achieved by augmenting the reconstruction by placing a prosthesis beneath the transposed flap.

In several patients it became necessary to do a mastopexy in order to elevate the opposite breast to the level of the reconstructed breast. The reduction mammoplasty was used in several cases. As a rule, we tend not to do a reduction mammoplasty as the standard method of achieving symmetry.

In three patients, the definition of the inframammary fold was insufficient to produce a pendulous appearing breast. The fold had to be defined and some of the bulky fat removed from the lower thoracic area by suction-assisted lipectomy. We have not had this problem in recent cases. It has been obviated by clearly defining the inframammary fold as the initial step in creating the mound. Once the fold is created, the shaping of the skin and fat can be done to complete the reconstruction. Fullness in the lower thoracic region due to the presence of the muscle contained in the transfer, will still be noted. This fullness will gradually disappear as the muscle atrophies.

The question of patient acceptance of the procedure is of paramount importance since the procedure is one of some magnitude. Our experience has been that patients have accepted this method as one which produces a fairly normal appearing breast that maintains the feel of normal tissue: that is, the mound is soft and moves in a manner similar but not fully equal to the remaining breast. The removal of a single rectus abdominis muscle unit does not appear to detract from the patients ability to do ordinary tasks. Diminution in strength of the abdominal wall has not been a complaint, or at least its presence has been an acceptable trade off for the reconstruction. I have not had experience with the use of both rectus abdominis muscle pedicles, but reports in-

dicate that considerable weakness of the abdominal wall does occur when both muscles are sacrificed.

It is our practice to have prospective patients for TRAM reconstruction speak to others who have had the surgery before making up their minds. They are informed of all of the procedures that are available for their specific reconstructions, and are put in contact with patients who have had them. The encounters give the patient the opportunity to ask questions and to receive answers that only another person who has experienced the reconstruction can give. A patient who is prepared in this manner and accepts the operation, becomes an informed participant in the operation deemed appropriate for her reconstruction.

It is our practice to have prospective patients for TRAM reconstruction speak to others who have had the surgery before making up their minds.

The free flap method of tissue transfer has recently been applied to breast reconstruction. The rectus abdominis musculocutaneous flap, the superior gluteal flap and a lateral thigh flap have been carried on their vascular pedicles, transposed to the thorax, and then revascularized by utilizing the techniques of microvascular surgery.¹⁵⁻¹⁷

Summary

Today there are many types of reconstruction available for the patient with a post-mastectomy deformity. Experience with all the types enables the surgeon to select the one that is appropriate to the particular reconstruction. The TRAM flap method is one which has proven to be an excellent method in selected cases. It is one

that can result in the reconstruction of an attractive breast, yet be done with an acceptable risk of surgical complication.

References

- ¹ Lapin R et al: Primary breast reconstruction following mastectomy using a skin expander prosthesis, *Breast* 6:97, 1980.
- ² Radovan C. Tissue expansion in soft-tissue breast reconstruction. *Plast. Reconstr. Surg.* 74:482, 1984.
- ³ Tansini I.: Nuovo processo per l'amputazione della mammella per cancro, *Ref-orma Med.*, 12:3, 1896.
- ⁴ Schneider WJ, Hill HL Jr., and Brown RG. Latissimus dorsi myocutaneous flap for breast reconstruction. *Br. J. Plast. Surg.* 30:277, 1977.
- ⁵ Bostwick J, III, Vasconez LO, and Jurkiewicz MJ. Breast reconstruction after radical mastectomy. *Plast. Surg.* 61:682, 1978.
- ⁶ Robbins TH. Rectus abdominis myocutaneous flap for breast reconstruction. *Aust. N.Z. J. Surg.* 49:527, 1979.
- ⁷ Hartrampf CR, Schefflan M, and Black PW. Breast reconstruction with a transverse abdominal island flap: Anatomic and clinical observations. *Plast. Reconstr. Surg.* 69:216, 1982.
- ⁸ Gibney J: The long term results of tissue expansion for breast reconstruction, *Clin Plast Surg* 14:509, 1987.
- ⁹ Versaci AD: Reconstruction of a pendulous breast utilizing a tissue expander, *Clin Plast Surg* 14:499, 1987.
- ¹⁰ Versaci AD: Reconstruction of the breast utilizing a tissue expander, *Inst. Courses Plast Surg Educ Found* 2:182, 1989.
- ¹¹ Becker H: The permanent tissue expander, *Clin Plast Surg* 14:519, 1987.
- ¹² Kroll SS, Netscher DT: Complications for TRAM flap breast reconstruction in obese patients. 84:866, 1989.
- ¹³ Little JW, Spear SL: Nipple-areolar reconstruction and tattoo, *Inst. Courses Plast Surg Educ Found* 2:199, 1989.
- ¹⁴ Little JW: Nipple-areola reconstruction, *Clin Plast Surg* 11:351, 1984.
- ¹⁵ Fujino T, Harashina T, and Enomoto K. Primary breast reconstruction after a standard radical mastectomy by a free flap transfer. *Plast. Reconstr. Surg.* 58:371, 1976.
- ¹⁶ Serafin D, and Georgiade NG. Transfer of free flaps to provide well-vascularized, thick cover for breast reconstructions after radical mastectomy. *Plast. Reconstr. Surg.* 62:527, 1978.
- ¹⁷ Shaw, WW. Breast reconstruction by superior gluteal microvascular free flaps without silicone implants. *Plast. Reconstr. Surg.* 72:490, 1983.

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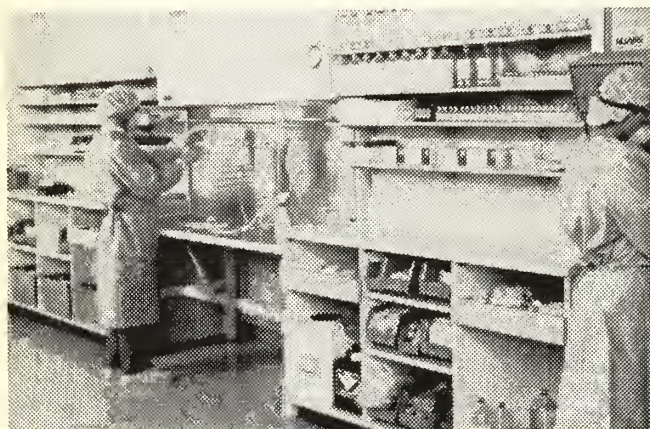
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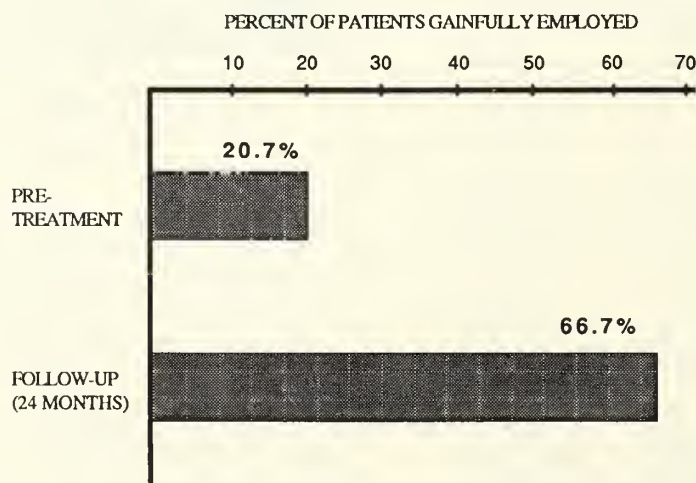
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Primary Extranodal Non-Hodgkin's Lymphoma of the Extrahepatic Biliary Tract

George N. Tzanakakis, MD
Michael P. Vezeridis, MD
Benjamin T. Jackson, MD
Jesus V. Rodil, MD
Kilmer S. McCully, MD

... non-Hodgkin's lymphoma arising primarily from the biliary tree is a very uncommon entity and obstructive jaundice, as initial presenting symptom of lymphoma, is also infrequent.

Extranodal non-Hodgkin's lymphoma is a relatively common occurrence,¹⁻⁴ and lymphomatous infiltration of the liver and biliary tree are commonly seen in disseminated disease.¹ However, non-Hodgkin's lymphoma arising primarily from the biliary tree is a very uncommon entity,^{1,2,5,6} and

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obstructive jaundice, as initial presenting symptom of lymphoma, is also infrequent.^{1,7,8} We are reporting a case of extranodal non-Hodgkin's lymphoma arising from the extrahepatic biliary tract and extending into the pancreas with obstructive jaundice as the initial presenting symptom.

Case Report

A 70-year-old white male was admitted to the Providence Veterans Administration Medical Center on May 9, 1984 with the recent onset of jaundice. He had a history of

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diarrhea for one year and intermittent sharp left upper abdominal quadrant pain radiating to the back for two months. The pain usually occurred following meals and was relieved by vomiting. He had lost 20 lbs in the previous five months. His past medical history was remarkable for chronic alcohol abuse and atrial fibrillation, requiring cardioversion and digitalization. Remarkable findings on physical examination were icteric sclerae, an enlarged, non-tender liver extending 4cm below the right costal margin, and varicosities of the lower extremities. Abnormal laboratory findings included a white blood cell count of 16,100 with 32% polys, 8% bands, 44% lymphocytes, 4% monocytes, 1% eosinophils and 11% atypical lymphocytes. Bilirubin was 9.0 mg/dl with a direct component of 4.5 mg/dl, alkaline

ABBREVIATIONS USED:

CT: computerized tomography
SGOT: serum glutamic oxaloacetic transaminase
SGPT: serum glutamic pyruvic transaminase

phosphatase was 430 U/L, SGOT was 109 U/L, and SGPT was 68 U/L. Albumin was 3.7 g/dl. Ultrasonography of the right upper quadrant showed dilated intrahepatic and extrahepatic biliary ducts. A percutaneous transhepatic cholangiogram showed dilated right intrahepatic ducts, while the left intrahepatic duct failed to fill. The common bile duct showed a filling defect in the upper portion soon after exit from the liver. The distal common bile duct was slightly dilated and the dye was able to pass into the duodenum. A CT scan of the abdomen and pelvis showed a mass in the area of the head of the pancreas and the porta hepatis. The patient was subsequently referred to the Surgical Service and he underwent an exploratory laparotomy on May 15, 1984. At exploration, the head of the pancreas was edematous and large. There was thickening and fibrotic reaction around the head of the pancreas which extended over and around the extrahepatic biliary system. The common bile duct was identified with difficulty by dissecting sharply through hard, gritty tissue. A cholecystectomy was performed. Multiple biopsies were obtained from the periportal tissue and were sent for frozen section, which showed chronic inflammatory reaction with infiltrates of mononuclear cells.

Four transduodenal tru-cut needle biopsies of the pancreas were performed, and frozen section showed normal pancreas in all four specimens. An intraoperative cholangiogram showed a normal appearing distal common bile duct and an area of stenosis at the junction of the right and left hepatic ducts. A common duct exploration was performed and the stenosis of the proximal duct was dilated. A T-tube was placed into the common bile duct. Prior

to closing the abdomen, a wedge biopsy of the liver was obtained because it appeared cirrhotic. The post-operative course was relatively benign, and he was discharged on the 16th postoperative day. The final pathology report, following review of the permanent sections, was atypical lymphoid infiltrate consistent with malignant lymphoma. There was a diffuse, mixed small and large cell infiltrate involving portal tissue, gallbladder (fig. 1), peripancreatic tissue and liver. There was nodular regenerative hyperplasia of liver. He was started on chemotherapy with cyclophosphamide, vincristine, prednisone and adriamycin but following a short downhill course, he expired on September 15, 1984. An autopsy showed malignant lymphoma of the common bile duct also involving the head of the pancreas (fig. 2) porta hepatis (fig. 3) and liver. No evidence of lymphoma was found in the paraaortic, peripancreatic, porta hepatis, axillary, inguinal or mediastinal lymph nodes. The cause of death was bilateral bronchopneumonia.

Discussion

The interesting features of this case are the origin of lymphoma from the extrahepatic biliary tract and the initial presentation with obstructive jaundice. Both these features represent rare occurrences.^{1, 2, 5-8} Freeman et al² reviewed 1,467 cases of non-disseminated extranodal non-Hodgkin's lymphoma and found only 6 cases involving the liver and the biliary system and 9 cases involving the pancreas. The number of cases originating in the biliary tract is not specified in that report. The only well documented case of extranodal non-Hodgkins lymphoma arising from extrahepatic bile ducts was reported by Nguyen in 1982.¹ The pancreas is involved in the 1.3% of patients with intra-abdominal non-Hodgkin's lymphomas. The vast majority of these patients have massive periaortic or retroperitoneal lymphadenopathy.^{5, 6} Sporadic cases of isolated pancreatic and peripancreatic involvement have been reported in the literature.^{5, 9, 10, 11}

Obstructive jaundice is a rare initial manifestation of lym-

Figure 1. The mucosa of gallbladder wall is thickened and infiltrated by lymphoma cells. H and E $\times 190$.

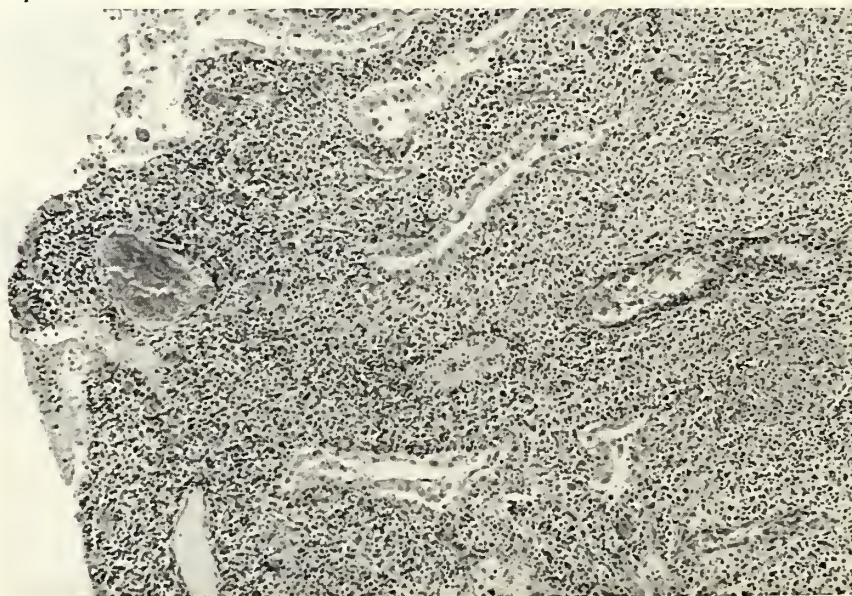
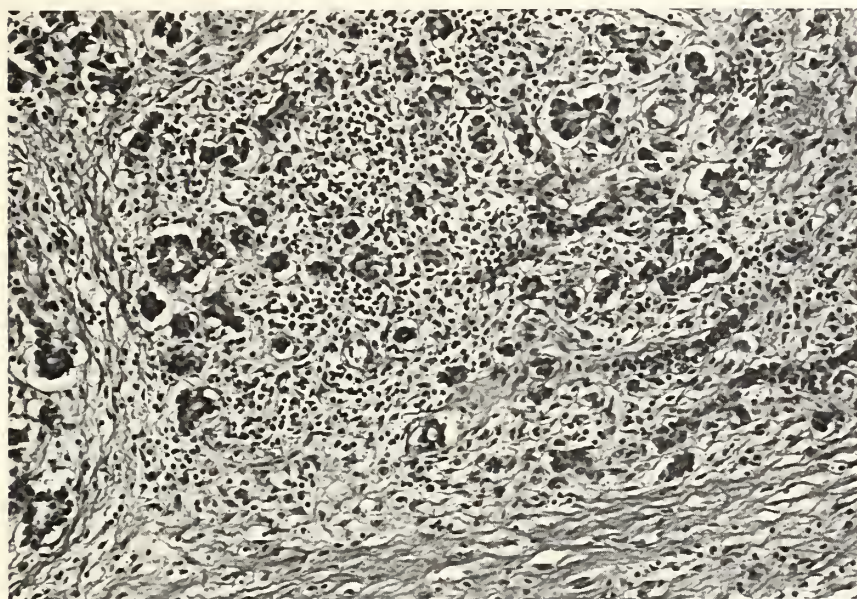


Figure 2. The pancreatic parenchyma is atrophic and infiltrated by lymphoma cells and foci of fibrosis. H and E $\times 190$.

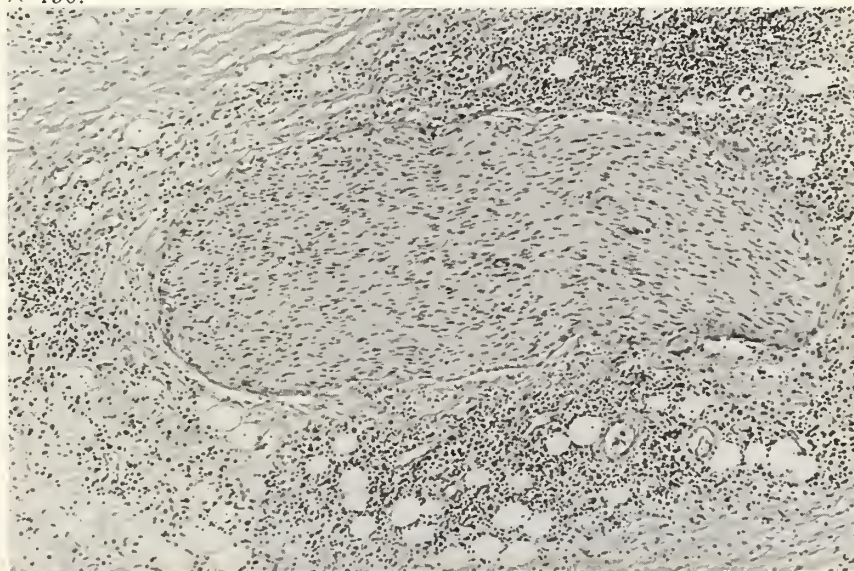


phoma.^{1, 7, 8} Rosenberg et al⁸ reviewed 1,269 patients with non-Hodgkins lymphoma and found only 3 patients presenting with obstructive jaundice. During the course of disseminated lymphoma, however, jaundice is less uncommon. Jaundice is most often encountered in patients with Hodgkin's disease and is associated with a poor prognosis. The pathogenesis of jaundice in lymphoma patients includes hepatitis, severe hemolysis, lymphomatous infiltration of the liver and biliary tree and compression of the extrahepatic bile ducts by enlarged lymph nodes.^{1, 7, 12, 13, 14} In a small percentage of patients, the etiology of jaundice is attributed to intrahepatic cholestasis of unknown pathogenesis.¹³ The jaundice in the case described in this report was most likely secondary to infiltration of the proximal common bile duct by lymphoma cells and fibrous tissue.

Lymphadenopathy was not present throughout the clinical course of this patient. Additionally, the extranodal origin of the lymphoma was confirmed by autopsy which showed no evidence

of disease in paraaortic, peripancreatic, porta hepatis, axillary, inguinal or mediastinal nodes. Timely diagnosis of extranodal lymphoma is significant, since the treatment is different and the prognosis better than that of nodal lymphoma or carcinoma.^{2, 15} The unusual initial manifestation of lymphoma with jaundice may be easily misdiagnosed as sclerosing cholangitis, common duct

Figure 3. The porta hepatis contains a hypertrophic nerve surrounded by fibrous tissue and adipocytes invaded by lymphoma infiltrate. H and E $\times 190$.



stone, cholangiocarcinoma or pancreatic cancer. Although rare, primary lymphoma should be considered in the differential diagnosis of obstructive jaundice.

Summary

A case of extranodal non-Hodgkin's diffuse, mixed small and large cell lymphoma of the extrahepatic biliary tract with jaundice as the initial manifestation is reported in this paper. Obstructive jaundice is very rarely an early symptom in lymphoma. The pathogenesis of jaundice in this case was infiltration of the extrahepatic bile duct by lymphoma cells and fibrosis.

References

1. Nguyen KG. Primary Extranodal Non-Hodgkin's lymphoma of the Extrahepatic Bile Ducts. Report of a case. *Cancer* 1982;50:2218-2222.
2. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972;29:252-260.
3. Banfi A, Bonadonna G, Carnevali G, Oldini C, Salvini E. Preferential sites of involvement and spread in malignant lymphomas. *Europ. J. Cancer*. 1968;4:319-324.
4. Modan B, Shani M, Goldman B, Modan M. Nodal and extranodal malignant lymphoma in Israel: an epidemiological study. *Brit. J. Haemat.* 1969;16:53-59.
5. Hart JM, White TT, Brown PC, Freeny PC. Potentially Curable Masses in the Pancreas. *Am. J. Surg.* 1987;154:134-136.

- ⁶ Boddie AW, Eisenberg BD, Mullins JO, Schlichtemeier AL. The Diagnosis and Treatment of Obstructive Jaundice Secondary to Malignant Lymphoma: A Problem in Multidisciplinary Management. *J. Surg. Oncol.* 1980;14:111-123.
- ⁷ Friedman CJ, Lambert MJ. Obstructive Jaundice as Initial Presentation of Non-Hodgkins Lymphoma: Value of Internal Percutaneous Transhepatic Biliary Drainage. *Southern Med. Journal* 1981;74:1005-1007.
- ⁸ Rosenberg SA, Diamond HD, Jaslowitz B, Craver LF; Lymphosarcoma: A review of 1269 cases. *Medicine* 1961;40:31-84.
- ⁹ Ackerman NB, Aust JC, Bredenberg CE, Hanson VA, Rogers LS. Problems in differentiating between pancreatic lymphoma and anaplastic carcinoma and their management. *Ann. Surg.* 1976;184:705-708.
- ¹⁰ Najem AZ, Porcaro JL, Rush BF, Jr. Primary non-Hodgkin's lymphoma of the duodenum. Case report and literature review. *Cancer* 1984;54:895-898.
- ¹¹ Young IF, Roberts-Thompson IC, Sullivan JR. Histiocytic lymphoma presenting with extrahepatic biliary obstruction: A report of three cases. *NZ J. Surg.* 1981;51:181-183.
- ¹² Levitan R, Diamond HD, Craven LF: Jaundice in Hodgkin's disease. *Am. J. Med.* 1961;30:99-111.
- ¹³ Bouroncle BA, Old JW, Jr., Vasques, AG: Pathogenesis of jaundice in Hodgkin's disease. *Arch. Intern. Med.* 1962;110:872-883.
- ¹⁴ Perera DR, Greene ML, Fenster LF. Cholestasis associated with extrabiliary Hodgkin's disease. Report of three cases and review of four others. *Gastroenterology* 1974;67:680-685.
- ¹⁵ Saltzstein SL: Extranodal malignant lymphoma and pseudolymphoma. *Path. Annu* 1969;4:159-184.

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40	\$13.21	\$20.13	\$ 35.94
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Myelomatous Pleural Effusion: Report of an Unusual Occurrence

Michael C. Brabeck, MD
Gary Bubly, MD
Timothy J. Hunter, MS, MD
Rogers C. Griffith, MD

Involvement of non-reticuloendothelial tissue is infrequent (in myeloma), and pleural involvement is very uncommon. . .

First reported nearly 100 years ago,¹ extraosseous tissue involvement in multiple myeloma is common, occurring with an incidence of approximately 75% in autopsy series. In the majority of cases, extraosseous myeloma is

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limited to reticuloendothelial tissue, usually spleen, lymph nodes, and liver.^{2,3} Involvement of non-reticuloendothelial tissue is infrequent, and pleural involvement is very uncommon, only 35 cases having been previously reported in the world literature (references available on request). Cases of simultaneous pleural and peritoneal⁴ and pleural and meningeal involvement have been reported.

In their review of thoracic and pulmonary abnormalities in multiple myeloma, Kinzer et al found pleural effusion in 6% of 958 patients.⁶ The most common etiology of pleural effusion was congestive heart failure caused by amyloidosis or presumed atherosclerotic coronary artery disease. Intermediate in frequency was infection, followed by pulmonary infarct. Myeloma alone was the least common cause of pleural effusion, occurring in 0.8% of the patients studied. We report the case of a patient who developed a left pleural effusion with treated myeloma as a result of diffuse thoracic extramedullary myelomatous infiltration.

Report of a Case

The patient was a 68-year-old

white male who presented in March, 1987, with upper abdominal pain thought initially to be of biliary origin. He was noted to be mildly leukopenic (WBC $3.3 \times 10^9/L$), but complete blood count was otherwise normal. Alkaline phosphatase was 57 U/L. Roentgenograms of the chest and abdomen, ultrasound examination of the right upper quadrant, oral cholecystogram, upper gastrointestinal endoscopy, and computerized axial tomography of the abdomen were unremarkable. The abdominal pain subsided, but in May low back pain appeared, and roentgenograms of the lumbar and thoracic spine showed a minimal compression fracture of T8. In June, nausea, vomiting, and weight loss developed and he was admitted to the hospital where he was found to be dehydrated with a hematocrit of 0.29 and a serum calcium of 3.67 mmol/L (14.7 g/dL). Serum protein electrophoresis showed a total protein of 91

ABBREVIATIONS USED:

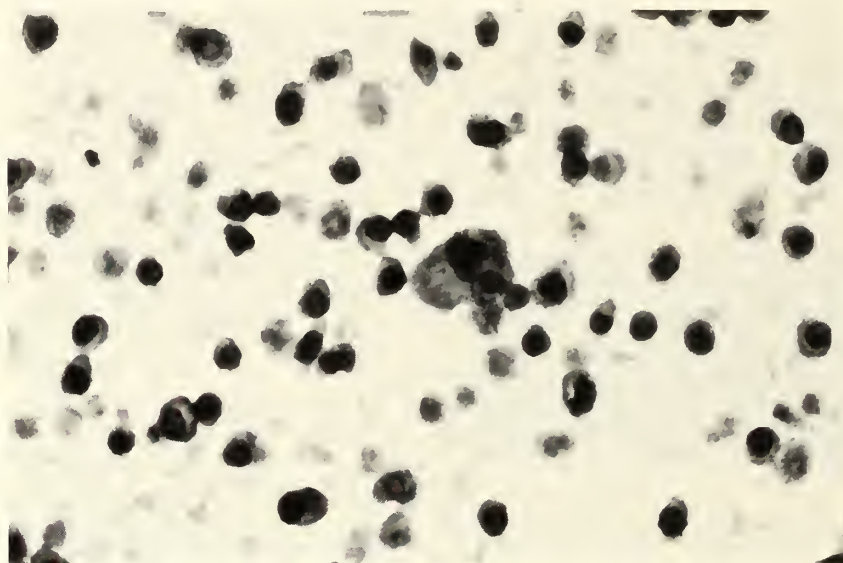
*IgA: immune globulin A
IgD: immune globulin D
L3: lumbar vertebra three
T8: thoracic vertebra eight*

g/L (9.1 g/dL) with a spike in the gamma region totaling 31 g/L (3.1 g/dL). Serum protein immunoelectrophoresis revealed an IgA lambda paraprotein, the quantitative analysis of which yielded 17g/L (1701 mg/dl). A radiographic bone survey did not show lytic lesions, but suggested a paravertebral mass at T8. This was presumed to be a plasmacytoma and not biopsied. Bone marrow biopsy from the iliac crest confirmed the diagnosis of multiple myeloma, showing 70-80% poorly differentiated plasma cells. Treatment was begun with melphalan and prednisone.

He did well, with complete resolution of all signs and symptoms of disease until July, 1987, when he again developed upper abdominal pain, this time accompanied by right lower extremity pain and weakness, including foot drop. He was found to have several lytic lesions in the lumbar and thoracic vertebrae as well as spinal stenosis at L3, and radiation therapy was empirically directed to the paravertebral mass at T8 and to the cauda equina region with prompt symptomatic improvement.

He then remained clinically well until December, when he noted the onset of a nonproductive cough. Chest X-ray showed a large, left pleural effusion. Computerized axial tomography of the chest revealed bilateral pleural effusions and a small pleural based density abutting a rib in the left anterior chest. Lytic lesions of the ribs were not seen. Left thoracentesis yielded pleural fluid with a total protein of 37 g/L (3.7 g/dL), 5×10^{10} RBC/L, and 6.6×10^9 WBC/L. All of the latter were abnormal plasma cells (Fig. 1). Pleural fluid protein electrophoresis showed a gamma spike of 7.7 g/L (0.77g/dl) and immunoelectrophoresis demonstrated a monoclonal IgA lambda paraprotein.

Figure 1. Smear of pleural effusion demonstrates numerous abnormal plasma cells including binucleate, nucleolated, and pleomorphic forms. (Wright's stain, magnification 400 \times)



tein. Another bone marrow biopsy showed 40-50% abnormal plasma cells. Radiographic bone survey now showed lytic lesions in the pelvis, right humerus, left femur, and a recent subcapital fracture of the right femur. Chemotherapy was begun with vincristine, adriamycin, and dexamethasone. Radiation therapy was directed to his painful right humerus and left femur.

His final admission was in January, 1988, for a second course of vincristine, adriamycin, and dexamethasone. His left pleural effusion had increased and a chest tube was inserted for symptomatic relief. Respiratory distress worsened and he expired after a brief course. Autopsy revealed extraosseous myeloma involving the hilar lymph nodes, liver, and spleen. There was diffuse myelomatous infiltration of the visceral and parietal pleura. Neither peritoneal nor meningeal involvement was found.

Discussion

When myeloma is the sole cause of pleural effusion, autopsy usually reveals either pleural infiltra-

tion from disseminated intramedullary myeloma, as in our patient, or an extramedullary plasmacytoma. The mechanism of pleural fluid formation is speculative, but probably involves the production of large quantities of immunoglobulins by malignant plasma cells in or near the pleura, thereby increasing the colloid oncotic pressure of the pleural space to a degree which impedes the normal reabsorption of fluid.⁷

There are several case reports of the successful resolution of myelomatous pleural effusion following systemic chemotherapy.

Successful treatment of myelomatous pleural effusion may be difficult. Local irradiation and pleurodesis have been used infrequently, usually with poor results. Theoretically, chemotherapy seems more attractive, since a successful response to chemotherapy includes a significant reduction in the monoclonal protein produced by the malignant cells, thus favoring the reabsorp-

tion of pleural fluid.⁷ There are several case reports of the successful resolution of myelomatous pleural effusion following systemic chemotherapy.^{4, 7-10}

For unclear reasons, myelomatous pleural effusion is usually left sided, although on occasion it may be bilateral. Also unexplained is the preponderance of IgA myeloma in reported cases of myelomatous pleural effusion; although it accounts for only 25% of all types of multiple myeloma, the incidence of IgA myeloma in such effusion is well over 50%. An interesting speculation is that the well known tendency of IgA protein to polymerize may in some way impede adequate drainage of fluid from the pleural cavity. The next most frequently occurring myeloma type is IgG; 3 cases of IgD¹¹ and 2 cases of light chain myeloma^{5, 12} have also been reported.

... the appearance of myelomatous pleural effusion ... is usually regarded as a poor prognostic sign, death usually occurring within 4 months of detection.

The importance of accurate diagnosis of the cause of pleural effusion occurring during the course of multiple myeloma is obvious; appropriate treatment is based upon the underlying cause. Fortunately, the diagnosis of myelomatous effusion is usually straightforward: diagnostic thoracentesis with immunocytochemistry is sufficient in most cases.^{13, 14} Ancillary maneuvers such as immunoelectrophoresis of the pleural fluid protein, pleural biopsy, and immunoglobulin histochemistry or gene rearrangement studies are occasionally useful when the etiology of the effusion remains obscure.

Myelomatous pleural effusion

may be a presenting sign of the disease,^{9, 15} but more typically, as in our patient, who survived 6 weeks after its appearance, it is a late manifestation. Although one patient is reported to have survived 30 months after the appearance of myelomatous pleural effusion,⁴ its presence is usually regarded as a poor prognostic sign, death usually occurring within 4 months of detection.

Summary

Pleural effusion complicating the course of multiple myeloma is common. Myelomatous pleural effusion, in contrast, is distinctly rare. Searching the Medline data base, a total of only 35 previously reported cases could be located. A recent case we cared for prompted us to review the literature in this area. The incidence of myelomatous effusion, possible mechanisms of its formation, and implications for therapy and prognosis are discussed.

References

- ¹ Kudrewsky B: Ztschr Heilk 1892;13:300.
- ² Churg J, Gordon AJ: Multiple myeloma lesions of the extraosseous hematopoietic system. Am J Clin Pathol 1950;20:934-45.
- ³ Hayes DW, Bennett WA, Heck FJ: Extramedullary lesions in multiple myeloma: Review of literature and pathologic studies. Arch Pathol 1952;53:262-73.
- ⁴ Estrov Z, Berrebi A, Hazani E, Peretz P: Pleural effusion and ascites as presenting signs of IgA myeloma. Haematologica 1973;68:104-9.
- ⁵ Witt DH, Zalusky R, Castella A, Mercer WD: Light chain myeloma with meningeal and pleural involvement. Am J Med 1986;80:1213-16.
- ⁶ Kintzer JS, Rosenow EC, Kyle RA: Thoracic and pulmonary abnormalities in multiple myeloma: A review of 958 cases. Arch Intern Med 1978;138:727-30.
- ⁷ Waddell CC, Waddell LC: Response of myelomatous pleural effusion to chemotherapy. Chest 1981;81:765-6.
- ⁸ Scullin DC, Cohen HJ: Myelomatous pleural effusion. Clinical course and immunologic characterization of the pleural fluid cells. Am J Hematol 1979;6:267-73.
- ⁹ Shoenfeld Y, Pick AI, Weinberger A, Ben-Bassat M, Pinkhas J: Pleural effusion-presenting sign in multiple myeloma. Respiration 1978;36:160-4.
- ¹⁰ Badrinan F, Rodriguez-Roisin R, Rives A, Picado C: Multiple myeloma with pleural

involvement. Am Rev Respir Dis 1974;110:82-7.

¹¹ Kamal MK, Williams E, Poskitt TR: IgD myeloma with malignant pleural effusion. South Med J 1987;80:657-8.

¹² Kwan WC, Lam SC, Klimo P: Kappa light-chain myeloma with pleural involvement. Chest 1986;86:494-6.

¹³ Kapadia S: Cytological diagnosis of malignant pleural effusion in myeloma. Arch Pathol Lab Med 1977;101:534-5.

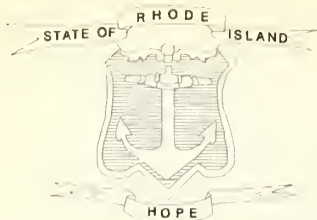
¹⁴ Angrish K, Dawar R, Verma K: Malignant pleural effusion in myeloma: Cytologic diagnosis. Indian J Pathol Microbiol 1980;23:267-71.

¹⁵ Kleinholz EJ, Tennebaum MJ: Pleural plasmacytoma presenting as pleural effusion. Va Med Mon 1973;100:1035-40.

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HEALTH BY NUMBERS

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H. Denman Scott, MD, MPH
Director of Health

Cancer in Rhode Island: Focus on Blacks

Blacks represent the largest racial minority in Rhode Island. Among all Rhode Island residents counted in the 1980 census, blacks accounted for 77% of all non-whites (including blacks, native Americans, and Asians), and outnumbered Hispanics (an ethnic group including blacks and whites) 27,584 to 19,707. Blacks comprised 2.9% of the Rhode Island population in 1980 (compared with 0.9% for native Americans and Asians, and 2.1% for Hispanics).¹

More than 100 primary malignant neoplasms are diagnosed among non-Hispanic black Rhode Islanders annually (Figure 1). In the first two years of the Rhode Island Cancer Registry (1987 and 1988), 233 primary malignant neoplasms were reported for non-Hispanic black residents of the state. In the same period, only 63 primary malignant neoplasms were reported for Hispanics, Asians, and native Americans.

Among the five cancers most commonly reported for non-Hispanic blacks in 1987-1988 (representing 55% of all reports), colorectal cancer ranked first, followed by cancers of the lung, breast, prostate, and cervix (Figure 2). In comparison, among the five cancers most commonly reported for non-Hispanic whites in 1987-1988 (representing 60% of all reports), colo-rectal cancer ranked first, followed by cancers of the breast, lung, prostate, and bladder. There are two notable differences in these rankings. First, lung cancer ranked higher

than breast cancer for blacks, lower than breast cancer for whites. Second, cancer of the cervix was among the top five sites for blacks, but not for whites. Additionally, cancer of the prostate accounted for 9% of all cases reported for blacks, compared to 8% of all cases reported for whites. These observations reflect longstanding differences between black and white cancer rates nationally. Blacks suffer disproportionately from cancers of the lung, cervix, and prostate.²

The National Black Leadership Initiative on Cancer (NBLIC), a newly formed coalition supported by the National Cancer Institute, has selected cancers of the breast and prostate as targets for mortality reduction in the black community. In Rhode Island, the age-standardized death rate³ for breast cancer among females is 12% higher among blacks (all blacks, including those who identify themselves as Hispanic) than whites (all whites, including those who identify themselves as Hispanic), while the age-standardized death rate for prostate cancer among males is 113% higher among blacks than whites (Figure 3). Cancers of the breast and prostate are accessible to early detection and treatment. Screening for breast cancer with mammography and physical breast examination has been shown to reduce mortality from the disease by as much as 30%.⁴ The effectiveness of screening for prostate cancer with the digital rectal examination has not been

tested in prospective clinical trials, but the test has been shown to detect some tumors early, and the results of some studies suggest improved survival with early detection. The American Cancer Society and the National Cancer Institute recommend the test, while the US Preventive Services Task Force finds "insufficient evidence to recommend for or against routine digital rectal examination."⁵ The Rhode Island Department of Health is working with other organizations to build an effective cancer control effort in the black community, and maintains a liaison with NBLIC, to support and participate in their activities.

References

- ¹ United States Bureau of the Census: 1980 Census of Population. Volume 1, Characteristics of the Population. Chapter B, General Population Characteristics. Part 41, Rhode Island. US Census Publication PC80-1-B41. US Government Printing Office, Washington, 1982.
- ² National Cancer Institute: Cancer Statistics Review 1973-1987. NIH Publication 90-2789. National Cancer Institute, Bethesda, Maryland, 1990.
- ³ US Environmental Protection Agency and National Cancer Institute: Cancer Mortality Rates and Trends, 1950-1979. US Government Printing Office, Washington, 1983.
- ⁴ National Cancer Institute: Cancer Control Objectives for the Nation: 1985-2000. Bethesda, Maryland: US Department of Health and Human Services, Public Health Service, National Institutes of Health, 1986; DHHS publication no. (NIH) 86-2880. (NCI Monograph no. 2).
- ⁵ The US Preventive Services Task Force: Guide to Clinical Preventive Services. Williams and Wilkins, Baltimore, Maryland 1989.

Figure 1. Newly diagnosed malignant neoplasms, *in situ* and invasive cancers of all types, Rhode Island residents 1987-1988, by race and ethnicity

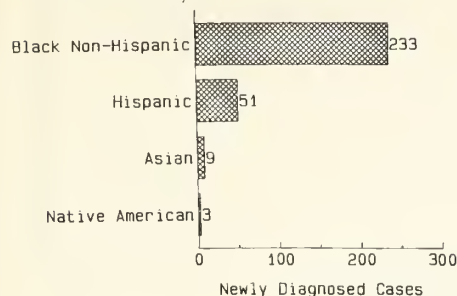


Figure 2. Newly diagnosed malignant neoplasms, *in situ* and invasive cancers of all types, Rhode Island residents 1987-1988, by race, ethnicity, and primary site, with a focus on the five most common primary sites

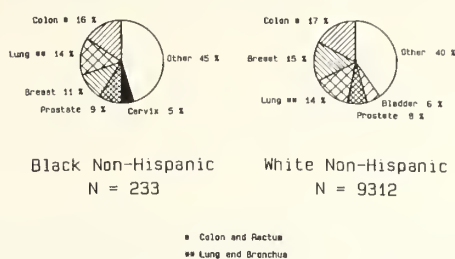
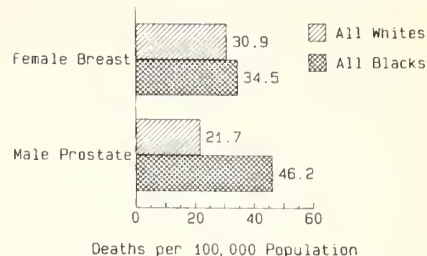


Figure 3. Age-standardized death rates from cancers of the female breast and male prostate, Rhode Island residents 1975-1985, by race



STATE OF RHODE ISLAND Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period June 1990 Number	12 Months Ending with June 1990	
		Number	Rates
Live Births	1,342	15,788	15.8*
Deaths	767	9,752	9.8*
Infant deaths	(13)	(152)	9.6†
Neonatal deaths	(11)	(122)	7.7†
Marriages	1,030	8,303	8.3*
Divorces	328	3,753	3.8*
Induced Terminations	677	7,858	497.7†
Spontaneous Fetal Deaths	106	1,203	76.2†
Under 20 weeks' gestation	(96)	(1,100)	69.7†
20+ weeks' gestation	(9)	(95)	6.0†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period June 1990 Number (a)	12 Months Ending with June 1990		
		Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	308	3,409	341.6	4,489.5
Malignant Neoplasms	197	2,411	241.6	6,404.0
Cerebrovascular Diseases	58	589	59.0	740.0
Injuries (Accident, Suicide, Homicide)	42	451	45.2	10,087.0
COPD	34	339	34.0	377.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 998,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

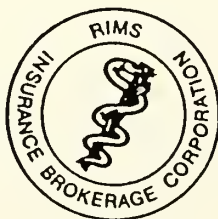
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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (October, 1940)

The lead article, written by E. S. Emery, Jr, MD of Boston, is entitled, "The Care of the Patient with Peptic Ulcer." The author stresses the three-fold nature of this therapy: 1. Treatment of the local condition; 2. Treatment of the patient's general health; and 3. Education of the patient concerning the nature of the disease. Success, the author contends, depends upon giving adequate attention to all three of these elements.

The author reviews his extensive experience in the care of patients with peptic ulcers. In 1929 he stated, "All evidence points to the fact that ulcer is a chronic disease and that all the present methods of treatment are merely palliative. Cure is probably rare." By 1935, following an intensive study of 1,435 patients, he stated, "... none of the present methods do more than assist in the induction of remissions, no matter how strict the medical schedule or how radical the operation."

Based upon his current experience with about 3,000 patients, the author maintains that the overwhelming majority of ulcer patients may be treated on an ambulatory basis "by methods which are available to any physician."

The first problem is to evaluate the severity of each case. "I have

learned to recognize types of patients who are always resistant to treatment. They have a severe degree of pain and frequently suffer from distress in the middle of the night. They show an unstable autonomic nervous system as manifested by a moist skin, particularly of the palms and they flush easily. They often exhibit the typical ulcer diathesis, or the lean and hungry look of Cassius. These individuals usually have a slight build and thin features with a pointed chin."

With regard to therapy, the author states: "The value of bland diets, which were originally prescribed empirically, has been demonstrated experimentally by Ivy and clinically by Soper, so that their use is indicated provided that the diet is well balanced as regards protein, carbohydrate and fat and contains sufficient calories and vitamins. Frequent feedings serve to relieve discomfort as do small doses of alkalis." In terms of newer medications, the author advocates the use of colloidal aluminum hydroxide.

The author concludes: "... the treatment of peptic ulcer is divided into those measures which affect the local conditions and those measures which benefit or control the general health of the patient. The type of local treatment will vary with the severity of the disease in the particular pa-

tient under consideration. The choice of local treatments consist of bland diets with frequent feedings, the object of which is to relieve distress, complete neutralization of the gastric acidity and surgery. Ultimate success in the treatment of this disease demands that every patient shall be educated regarding the nature of his disease and receive careful instructions concerning his general health, particularly as to nervous tension, infection and fatigue."

Albert H. Miller, MD, managing editor of the *Journal*, writes an historic review of Dr Usher Parsons touching particularly on his role in founding the Rhode Island Hospital. Parsons, born in Maine in 1788, was licensed as a practitioner of medicine, in Massachusetts, in 1811. In July of 1812, he was commissioned as a surgeon's mate in the US Navy, and served with distinction in the battle of Lake Erie under the command of Captain Oliver H. Perry. After the War of 1812, Parsons remained in the navy and was stationed in the Mediterranean for two years. He returned to the states, undertook further studies at Harvard Medical School and was awarded the MD degree in 1818. Following an extensive tour of European hospital facilities (during which time he strengthened collegial friendships with Duputren, DuBois, Pinel, Gay-

Lussac, Abernethy and Humphrey Davy), Parsons returned to the states and accepted the professorship of anatomy and surgery at Brown University. He lived first on Benefit Street and later on Waterman Street and conducted an active local practice in medicine and surgery. He served as president of the Providence Medical Association, the Rhode Island Medical Society, was instrumental in the founding of the American Medical Association and served as its vice president. In 1851, while president of the Providence Medical Association, Parsons formed a committee to study the need for a general hospital "... because of the amount of suffering and destitution that called loudly for hospital relief." The idea lay dormant for over a decade largely because no citizen volunteered to head the effort. In March of 1863, the General Assembly of Rhode Island finally authorized the incorporation of Rhode Island Hospital by 12 physicians headed by Usher Parsons and through the generosity of the Ives family, the initial construction funds were made available. Usher Parsons was 75 years of age when construction work was started on the hospital and he was present at the opening exercises on October 1, 1868. Nine days later the first operation was performed at the hospital (the removal of a cancerous growth of the mandible) with Parsons observing the procedure. Parsons died a few weeks later at age 80. (Ed. Note: *The definitive biography of Usher Parsons, "Yankee Surgeon: The Life and Times of Usher Parsons," published in 1988, is authored by Dr Seebert J. Goldowsky, Editor Emeritus of the Journal.*)

A brief item notes that the US death rate for 1939 (10.7 deaths per 1,000) is slightly more than the 1938 rate of 10.6 per 1,000.

Rhode Island's 1939 death rate is 11.4 per 1,000. (Ed. Note: *During the decade of 1980-89, the US death rate is 8.6 and for Rhode Island, 9.6 per 1,000.*)

The report of the Committee on Maternal Mortality is published in this issue of the *Journal*. There are 40 deaths associated with pregnancy (34 of puerperal causes and 6 of non-obstetrical causes) during 1939 with the following distribution: septic abortion [2]; abortion with hemorrhage [3]; ectopic pregnancy [1]; placenta previa and other hemorrhages [5]; puerperal sepsis [7]; eclampsia and other toxemias [9]; puerperal phlegmasia alba dolens and embolism [1]; accidents of pregnancy [6].

A notice from the State Department of Health declares the availability of free sulfapyridine for "... the treatment of any reported case of gonorrhea. . . ." The Department's policy of freely distributing antisyphilitic drugs remains unchanged. Arsenicals and bismuth preparations are freely available "... to any registered physician for the treatment of a report case."

* * *

Twenty Five Years Ago (October, 1965)

This issue of the *Journal* summarizes an article entitled "Life or Death by EEG," published in the October 12, 1964 issue of the JAMA, which is written by H. Hamlin, a resident of Providence. The article recommends a set of conditions for the certification of brain death (in association with cardio-respiratory activity artificially sustained by artificial means) and includes: no spontaneous respiration for 60 or more minutes; no reflex response; flat EEG lines for at least 60 minutes of recording; and normal serum electrolytes. The Ham-

lin article states further, "Efforts at reanimation of victims with cardiac or pulmonary failure should be pursued only so long as the brain shares physiologic response together with heart and lungs." (Ed. Note: *This remarkable article by Hamlin was written 13 years before the first federal committee was convened to establish criteria for cerebral death.*)

A special note is entitled, "Clinical Laboratories and the Practicing Physician — An Ethical Relationship and is authored by T. B. Casey and the Board of Examiners in Medicine (E. Kelly, M. DiMaio, J. Myrick). The article explores "... the occasional infringement of the legal limitations of the laboratory and the ethical relationship that should exist between it and physicians." The report concludes: "While it is true that a clinical laboratory is obligated by law to operate in an ethical manner and to avoid infringing on the areas of practice permitted only to licensed physicians, it is nevertheless appropriate to remind the medical profession of its obligations in its relationships with laboratories."

The lead scientific article, entitled "Treatment of Cardiac Arrhythmias" is written by S. Bellet, Professor of Cardiology, University of Pennsylvania. The article summarizes the numerous advances in the therapy of cardiac arrhythmias resulting from improved methods of diagnosis, expanding knowledge of the etiologic causes of arrhythmias, better employment of pharmacologic agents and the availability of newer mechanical and electronic devices such as pacemakers and cardioverters. The author concludes: "From the standpoint of the immediate therapeutic regimen, cardiac arrhythmias may be divided into three categories: [1] Slow heart rates, below 36 beats per minute (often associated with

hypotension), as in sinus bradycardia, partial or complete atrioventricular heart block, a slow idioventricular rhythm, or periods of cardiac arrest. [2] Heart rates ranging from 60 to 110 beats per minute, as in partial A-V heart block, atrioventricular dissociation, atrial flutter, or atrial fibrillation with varying degrees of atrioventricular block. [3] Heart rates ranging from 140 to 250 per minute, as in atrial or nodal tachycardia, atrial flutter, atrial fibrillation, or ventricular tachycardia.

"Many cases in the first group and most in the third require immediate therapy and often constitute a cardiac emergency. Urgent therapy is not ordinarily required with the second category. Time is available to study the patient. Since the rate does not deviate greatly from the normal, alterations in cardiovascular

dynamics due to a change in the heart rate are minimal. If digitalis toxicity is a factor, the rhythm will generally return to normal with omission of the drug."

An article by A. S. Glicksman is entitled "Combined Sequential Radiotherapy and Surgery in the Management of Malignancies." The author concludes: "Sufficient evidence has accumulated in the last quarter century for us to believe that the judicious association of radiation and surgery can improve our ability to control cancer. Properly designed prospective clinical trials based upon the very best surgical approaches to the particular cancer combined with the best planned precision radiotherapy available are not only possible and ethical but will prove most meaningful in the improvement of the management of malignant disease."

C. H. Hill writes a paper on "Cryosurgery in Otolaryngology" particularly in tonsillar disease. The author, summarizing his experience with 40 cases so treated, states: "The uses of cryotherapy are many. The advantages of decreased bleeding and office application warrant further investigation."

* * *

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Location: Le Meridien San Diego Coronado, California

For more information: Office of CME Sharp Memorial Hospital (619) 541-4530

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Sponsored by: Washington University, School of Medicine, St. Louis, Missouri

Date: November 1-3, 1990

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For more information: Office of CME, Washington University, School of Medicine, (800) 325-9862, (314) 362-6893

Title: Primary Care Update

Sponsored by: Interstate Postgraduate Medical Association

Date: November 12-15, 1990

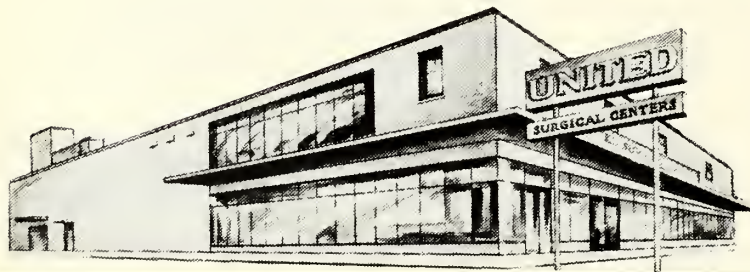
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**The Trustees of the Fiske Fund
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are pleased to announce the**

FISKE PRIZE FOR 1990

to be awarded for an original contribution submitted by licensed Rhode Island physicians. Eligible for the 1989 competition are original manuscripts not submitted elsewhere covering medical topics of a scientific, clinical, socio-economic, or historical nature. Submissions must be in English.

The award, initiated in 1836, is named after Caleb Fiske (1753-1834) who was a Rhode Island physician and judge, Army surgeon, and a descendant of Roger Williams.

Guidelines:

- 1) The original and one copy must be submitted by February 1, 1991 to Secretary, Caleb Fiske Fund, Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903.**
- 2) All papers must be double-spaced and should not exceed 10,000 words.**
- 3) The Trustees reserve the right to award one or more prizes.**
- 4) The award recipient(s) must transfer copyright privileges to the Trustees of the Caleb Fiske Fund of the Rhode Island Medical Society. The paper will be considered for publication in the *Rhode Island Medical Journal*, subject to review by the Editorial Board.**
- 5) The award recipient(s) will be presented with the prize amount, to be determined by the Board of Trustees of the Caleb Fiske Fund, at the Annual Meeting of the Rhode Island Medical Society to be held in May, 1991.**

Rhode Island Medical Society



STATEWIDE PHYSICIAN GROUP PURCHASING PROGRAM for RIMS Members

in cooperation with the Connecticut Health Institutional Services, Inc.

Based on national studies, the AMA estimates that the average solo practicing physician spends in excess of \$16,000 annually on office supplies and equipment. In the belief that Group Purchasing can accomplish significant savings for its members, The Rhode Island Medical Society, utilizing the experience and expertise of the Connecticut Health Institutional Services, Inc. (An affiliate of the Connecticut Hospital Association), identified areas of need and critically examined a number of companies.

The following firms have signed agreements with the RIMS Group Purchasing Program and meet the Society's strict standards for

Quality, Price and Service:

ARI Business Products, Ltd.	Office Equipment
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Bookmart	Books, Periodicals and Medical Reference Books
E. M. Parker Co., Inc.	X-ray Film Products/Services
General Medical Corporation	Medical/Surgical Supplies
Hartford Office Supply Co., Inc.	Office Supplies
Henry Schein, Inc.	Medical Sales
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RIMS Member Physicians interested in benefitting from group purchasing should contact Barbara Hicks at 331-3207.

Interactions *A Medical Staff Leadership Program*

**November 29, 1990
The Peabody Orlando
Orlando, Florida**

Medical staff leaders may find that their special clinical skills and extensive clinical experience do little to prepare them for the complexities of this demanding role. A role that requires the skills and sensitivity of an arbitrator, facilitator, manager, advisor, negotiator, communicator, problem solver, peacemaker and professional peer.

To help you refine your personal style of leadership, develop your professional decision-making and problem-solving abilities, and enhance your repertoire of management skills, the AMA is pleased to offer Interactions, the 1990 Medical Staff Leadership Program. It offers ample opportunity for leadership skill-building, self-assessment, frank conversation and feedback.

Program Participants

If you are a new chief-of-staff, department director, committee chairman or you serve in any other leadership capacity, the AMA's new Interactions can provide you with the self-assurance and skills you need to be successful in this challenging new role.

Leadership Objectives

- Improve emerging medical staff leaders' understanding of skills needed to perform formal duties.
- Enhance the understanding of medical staff leadership conflicts inherent in today's healthcare scene.
- Increase ability to interact effectively with medical staff peers and hospital/governing body leadership.

Location and Date

The AMA Medical Staff Leadership Program will be conducted on Thursday, November 29, 1990, at the Peabody Orlando Hotel, in Orlando, Florida. For ease of accommodations and travel, the AMA offers the program one day prior to the 1990 Hospital Medical Staff Section Interim Meeting, and three days prior to the 1990 AMA Interim Meeting.

Registration

For immediate registration or information, call toll-free 1-800-621-8335. Please have your MasterCard or Visa ready.

Registration fee

AMA Member - \$275

Non-member - \$375



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INFORMATION FOR AUTHORS

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal*.

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½ × 11 inch firm typewritten paper, double-spaced throughout (including title page, text, acknowledgments, and references) with margins of at least one inch and using but one side of each page. Tables, charts, and legends should be submitted separately from the text, and referred to by number (ie, Fig. 1) within the text. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title Page: All manuscripts must include a title page which provides the following information: (1) a concise and informative title; (2) the name of the author or authors with their highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointment, and primary hospital affiliation; (4) mailing address and office telephone of principal author; (5) mailing address of author responsible for correspondence or reprint requests; (6) source of support if applicable.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white 5 × 7 glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in the text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten on a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be appropriately masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive numbers of illustrations. Color plates are not acceptable.

Identification of Patients: Names, initials should not be used. Use of numbers is a preferable form of identification.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications will be undertaken so as to bring them into conformity with *Journal* style, which is in compliance with the editorial standards of the AMA. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal*.

Permission: When material is reproduced from other sources, full credit must be given both to the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: To conserve space and expense, references should be limited to those essential to the subject. The editor reserves the right to reduce the number when it is deemed necessary. The references must be double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

Correspondence: All correspondence relating to publication should be addressed to: Managing Editor, *Rhode Island Medical Journal*, 106 Francis Street, Providence, RI 02903.



VASOTEC

(ENALAPRIL MALEATE) MSD

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Contraindications: VASOTEC® (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor.

Warnings: Angioedema. Angioedema of the face, extremities, lips, tongue, glottis, and/or larynx has been reported in patients treated with ACE inhibitors, including VASOTEC. In such cases, VASOTEC should be promptly discontinued and the patient carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL), should be promptly administered.** (See ADVERSE REACTIONS.)

Hypotension: Excessive hypotension is rare in uncomplicated hypertensive patients treated with VASOTEC alone. Patients with heart failure given VASOTEC commonly have some reduction in blood pressure, especially with the first dose, but discontinuation of therapy for continuing symptomatic hypotension usually is not necessary when dosing instructions are followed; caution should be observed when initiating therapy. (See DOSAGE AND ADMINISTRATION.) Patients at risk for excessive hypotension, sometimes associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death, include those with the following conditions or characteristics: heart failure, hypotension, high-dose diuretic therapy, recent intensive diuresis or increase in diuretic dose, renal dialysis, or severe volume and/or salt depletion of any etiology. It may be advisable to eliminate the diuretic (except in patients with heart failure), reduce the diuretic dose, or increase salt intake cautiously before initiating therapy with VASOTEC in patients at risk for excessive hypotension who are able to tolerate such adjustments. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients at risk for excessive hypotension, therapy should be started under very close medical supervision and such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril or diuretic is increased. Similar considerations may apply to patients with ischemic heart disease or cardiovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of VASOTEC, which usually can be given without difficulty once the blood pressure has stabilized. If symptomatic hypotension develops, a dose reduction or discontinuation of VASOTEC or concomitant diuretic may be necessary.

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: General Impaired Renal Function. As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Oosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggestive of angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta-adrenergic-blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine, prazosin, and digoxin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radioactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not

been clearly defined, VASOTEC® (Enalapril Maleate, MSD) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome. Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed in utero to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypotension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of ¹⁴C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2987 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were: headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were: dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were: fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), and anorexia (1.5%). Nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring since the drug was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients (see WARNINGS, Hypotension), pulmonary embolism and infarction, pulmonary edema, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis (hepatocellular or cholestatic jaundice), melena, anorexia, dyspepsia, constipation, glossitis, stomatitis, dry mouth.

Musculoskeletal: Muscle cramps.

Nervous/Psychiatric: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Respiratory: Bronchospasm, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, anosmia, tinnitus, conjunctivitis, dry eyes, tearing.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgias/arthritis, myalgias, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 11% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol %, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: Hypertension. In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed. If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Oosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium (see PRECAUTIONS).

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance > 30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 2.5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure who have hyponatremia (serum sodium < 130 mEq/L) or with serum creatinine > 1.6 mg/dL, therapy should be initiated at 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d. then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more, if at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function. The maximum daily dose is 40 mg.

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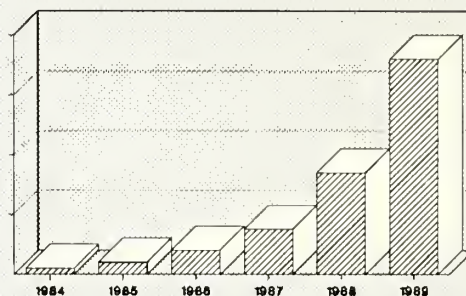


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Cover: The cover illustration is a drawing by Honoré Daumier, appearing in the September 11, 1844 issue of *le Charivari*. The legend states: "A Lucky Find. By gosh, I am delighted! You have yellow fever (*la fièvre jaune*) . . . it will be the first time that I have been lucky enough to treat this disease!"

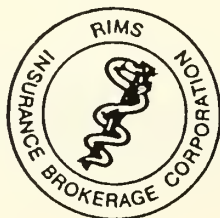
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EDITORIALS

Recent Advances in Internal Medicine

Recent scientific accomplishments in seven subspecialties of internal medicine are presented in this issue of the *Rhode Island Medical Journal*. The editors asked several hospital-based and office-based physicians to discuss selected topics which they regard as important both for themselves and for all practitioners of medicine. We did not ask them to discuss specific subjects within their field but left such selections to their discretion.

It is of interest, but not unexpected, that four of the seven reviewed subspecialties contained major commentaries on AIDS. It is also of note that the research and clinical features of hepatitis were emphasized by both the infectious disease and gastrointestinal disease reviewers. The micro-organism, *Helicobacter pylori*, was also discussed in these two reviews. Drs Emgushov, Opal and Feller, coming from very different viewpoints, focussed on this bacterium as a bad actor in the peptic ulcer arena. The good news is that therapies have now been designed which may well lead to relief for ulcer sufferers because of our better understanding of enteric microbiology.

Not surprisingly, the utility of erythropoietin was highlighted both in the hematology and nephrology reviews. The increasing use of this growth factor has been noted recently and its dazzling success in improving the quality of life for renal failure patients is a triumph of genetic engineering

and clinical research. The reviewer of renal disease, Dr Rex Mahnensmith, chose to place this and other advances in a lucid, historical perspective and I believe that readers will enjoy learning how far dialysis and other kidney-related therapies have progressed.

The hormone analog, somatostatin, has caught the fancy both of endocrinologist and gastroenterologist in treating both common and rare problems in their respective fields. Our reviewers chronicle the use of this multipurpose drug.

Other topics which have been updated include: Tuberculosis, asthma, chronic obstructive pulmonary disease, lung cancer, vascular and interstitial lung disease, bone marrow transplantation, immunoglobulin therapy, multiple sclerosis and other autoimmune disorders, blood coagulation, diabetes, hyperglycemia, bleeding esophageal varices, ascites, liver transplantation, gallstones, gastrointestinal bleeding, aluminum intoxication, new bacterial and viral infections, and new antifungal, antiviral and antibacterial agents.

Finally, Dr Byron Waksman, an internationally acclaimed research immunologist, provides the *Journal* with a clear description of the evolving field of psychoneuroimmunology.

I believe that you will find the reviews to be well-written and enjoyable. With information over-

load so common today, it is a credit to our authors that they have managed to distill so much new and exciting data into readable and digestible essays.

Fred J. Schiffman, MD

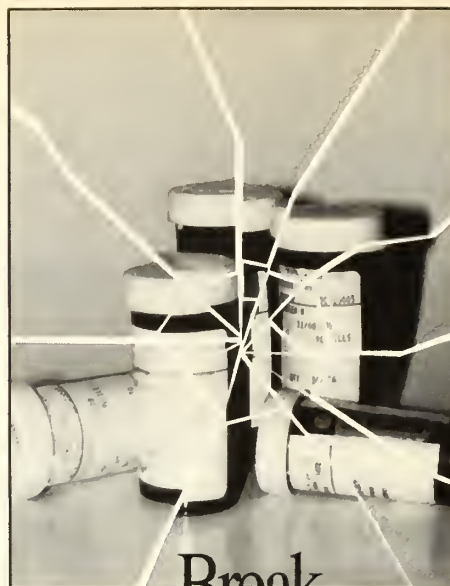
Upon the Shoulders of Giants

In a letter to Robert Hooke, written in the winter of 1676, Isaac Newton states: "If I had seen further than you and Descartes it is by standing upon the shoulders of giants." And if perchance the current practitioners of medicine see further, understand more deeply, the mysteries of human disease it is because they have been privileged to stand upon the shoulders of their predecessors who have labored to provide us with insight into these mysteries.

There were giants in the earth in those days says Genesis; but these giants were not only in Edinburgh or Leyden or Philadelphia or Boston: some had their origins in the smallest of the states, Rhode Island. From time to time, then, the *Rhode Island Medical Journal* will summarize the lives of our more gifted sons and daughters who have provided us with some light in the dark places of medicine.

The life and accomplishments of Nathan Smith, MD, born in what is now East Providence and the father of four New England medical schools, will be described in the December, 1990, issue of the *Journal*. In subsequent issues, the lives and contributions of yet other Rhode Island leaders of medicine such as Solomon Drowne, born in Providence, and Benjamin Waterhouse, born in Newport, will be summarized.

Stanley M. Aronson, MD



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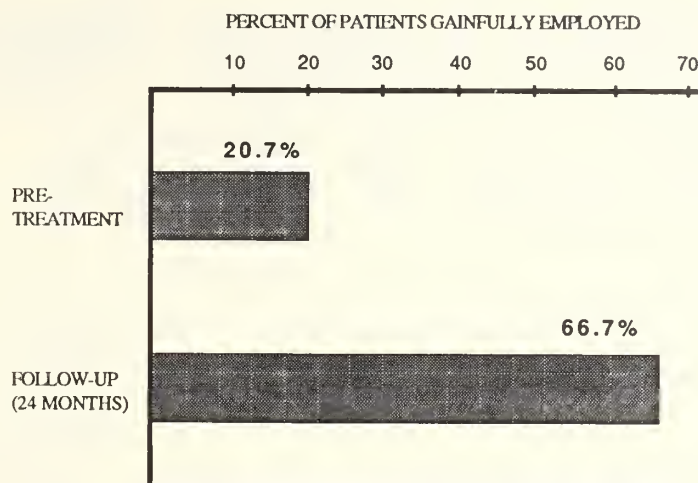
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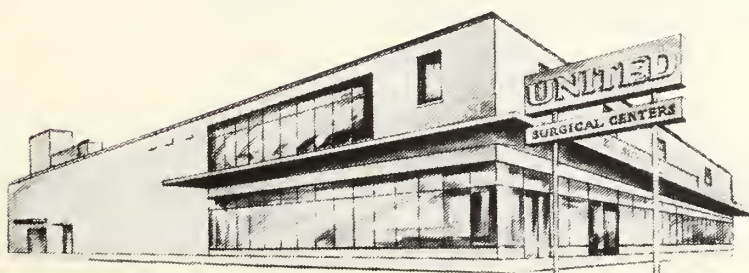
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Advances in Nephrology: A Selected Review of Progress in Care of the Patient with Renal Failure

Rex L. Mahnensmith, MD

... if repeated vascular access could be atraumatically and aseptically achieved, then repeated and even chronic maintenance dialysis would be feasible.

Nephrology emerged as a specialty in the 1950s as dialytic therapy and renal transplantation became viable therapeutic modalities for the patient with renal failure. This essay focuses on the progress made in these areas over the past several years, and highlights significant recent advances.

Progress with Hemodialysis

It was in 1836 that Richard Bright wrote this poignant description of the patient afflicted with end stage renal failure and uremia:

"He is usually subject to constant recurrence of his symptoms; or again, almost dismissing the recollection of his ailment, he will be suddenly seized with an

attack of pericarditis, or with a still more acute attack of peritonitis, which without any renewed warning, (may) deprive him in eight and forty hours of his life. Should he escape this danger, ... other perils await him; his headaches ... become more frequent; his stomach more deranged; his vision indistinct; his hearing depraved; he is suddenly seized with a convulsive fit. . . . He struggles through the attack, but again and again it returns; and before a day or a week has elapsed, worn out by convulsions, . . . overwhelmed by coma, the painful history of his disease is closed."¹

For more than a century following this classic description, no effective therapy existed for the patient with renal failure. The diligent physician would search for reversible etiologies of renal failure, such as obstruction of the urinary tract, or hope for a reprieve if the cause was an acute infection, but most commonly, the physician could only provide

comfort while the patient lay dying. Death was at times agonizingly slow, at times rapid and dramatic; at times the final days were peaceful, but often, the stupor was punctuated by convulsions, grimacing, fasciculations, repeated emesis, and pain from inflamed serosa.

It was in this context that thoughts regarding treatment of blood in order to remove accumulations of toxic waste materials began to appear in biomedical writings. As early as 1861, Thomas Graham, a chemist working in London demonstrated that water and urea could be separated from plasma when the plasma was layered across a stretched vegetable membrane. He termed this process "dialysis," and speculated that this

Rex L. Mahnensmith, MD, is Assistant Professor of Medicine at Brown University and Director, Division of Nephrology at The Miriam Hospital, Providence, Rhode Island.

ABBREVIATIONS USED:

CAPD: continuous ambulatory peritoneal dialysis
CNS: central nervous system
Epo: erythropoietin

technique might somehow be applied to the benefit of patients sick with uremia.²

Dialysis *in vivo* was first demonstrated in 1913 by John J. Abel from Johns Hopkins Medical School. Blood was rendered incoagulable with hirudin, a substance derived from leech saliva, and circulated extracorporeally through celloidin tubes suspended in a glass jacket of saline. With this first artificial kidney, Dr Abel was able to keep alive nephrectomized dogs for a few days. Due to many technical problems, his work was not carried forward to humans. In 1924, using improved celloidin tubes and a purer preparation of hirudin, George Haas of Germany performed the first human extracorporeal hemodialysis in a patient with acute renal failure. Over the next four years, Haas performed approximately one dozen hemodialyses, but none of his dialyses exceeded 60 minutes because of persistent problems with hirudin and the instability of the blood pressure, so overall therapeutic effect was limited. In the 1930s, two breakthroughs appeared: heparin became available for routine clinical use, and a new cellulose product named cellophane (a much sturdier semipermeable membrane than celloidin) was developed. Aware of these developments and having a special interest in the uremic patient, Willem Johan Kolff and Hendrik Berk of the Netherlands conceived of wrapping a 30 meter length of cellophane tubing around a drum, which hung partially immersed in a bath of saline. As this drum rotated, heparinized blood from a patient was propelled through the tubing, accomplishing extracorporeal hemodialysis. Though requiring over 750 milliliters of whole blood to prime the kidney, Kolff's rotating drum was successfully employed to treat acute

uremia and became a model for mass production. Over the ensuing 15 years, many hospitals acquired Kolff's dialyzers and successfully treated uremic patients. However, performance of consecutive dialyses in a given patient was limited by the difficulty in achieving repeated vascular access, which had to be accomplished by fresh arterial and venous cutdowns for each session. A patient would be fortunate to endure more than 10 cutdowns without sepsis, major hemorrhage, or major vessel thrombosis, so treatments were limited to those patients with an acute renal insult who were deemed to have either reversible renal failure or acute intoxications.²

Between 1950 and 1965, technical modifications of the artificial kidney were introduced which simplified treatment sessions and increased dialyzer efficiency. The Kolff rotating drum was modified to achieve higher clearance per hour but membrane ruptures and *ex vivo* clotting were common. With Travenol laboratories, Kolff then developed the twin coil dialyzer, which employed two membrane coils supported by wire mesh suspended in an open bath of dialysate. Blood flowed through the stationary coils while dialysate streamed around them. This new design stabilized the membranes which diminished rate of rupture and also improved clearance.

During this same period, the notion of a permanent vascular access germinated. To workers in the field, it seemed that if repeated vascular access could be atraumatically and aseptically achieved, then repeated and even chronic maintenance dialysis would be feasible. Many people worked on this most challenging problem, but the credit goes to Belding Scribner and Wayne Quinton (an engineer), then of

Seattle, who developed a precisely engineered Teflon arteriovenous external shunt as a method for obtaining repeated vascular access for dialysis.³ Teflon and silicone cannulae of hairpin design were inserted via cutdown surgery into the radial artery and cephalic vein and then anchored onto a stainless steel armplate further up the arm. Once in place, blood would circulate externally through the shunt from artery to vein. During dialysis, the shunt was opened at its middle where a sialastic connector existed. Minimal trauma ensued from this "Scribner shunt," and repeated access was feasible. At nearly the same time, Brescia and Cimino from New York described their concept of permanent vascular access — an arterialized vein created by direct anastomosis of the radial artery to the cephalic vein at the wrist.⁴ This Brescia-Cimino arteriovenous fistula has become the standard vascular access for the hemodialysis patient. At the time of their introduction, these inventions were landmark breakthroughs. Propelled by these advances, the Seattle group launched the world's first maintenance hemodialysis program and a new era in renal patient care was begun.

Now, almost 30 years have passed since the advent of maintenance dialysis. Worldwide, over 250,000 patients currently receive maintenance dialysis. Hemodialysis is not only allowing the patient with renal failure to live, it is restoring a quality of life which permits vocational pursuits and active participation in all aspects of life.⁵ Longevity with dialysis varies depending upon the age of the individual at initiation of dialysis and presence or absence of co-morbid diseases, such as diabetes mellitus and atherosclerotic heart disease. However, survival rates exceed 65% at 15 years

by some reports and can exceed 25 years.⁶ Near-perfect patient compliance, a positive outlook by the patient, constant physician surveillance and attention to detail, a reliable vascular access, control of hypertension, and expert input from the dialysis care team of nurses, dieticians, and social workers have proven necessary to the successful management and long-term survival of the dialysis patient.⁶

Throughout its history, progress with hemodialysis has been both conceptual and technologic, though it is probably fair to say that the innovations of greatest impact have been and continue to be technologic. For example, early dialysis machines employed an open bath design, where the dialyzer hung suspended in an open dialysate bath that required tedious manual preparation and repeated stirring. Bacterial growth in the water, cooling of the patient's blood, and low efficiency of clearance were issues. Dialysis times were 6-10 hours. Presently, hemodialysis is accomplished in a small closed-system cartridge through which freshly mixed dialysate and patient's blood pass by each other at rates exceeding 500 and 300 milliliters per minute, respectively. The most commonly employed dialyzers feature hollow capillary fibers situated in parallel, packed within a 10-12 inch cylinder that is 1.0 to 1.5 inches in diameter. Blood enters the cartridge at one end, then disperses into the thousands of capillary fibers which run the length of the cylinder. Dialysate streams into the cartridge through a side port, percolates among these fibers, then flows out. The dialysate itself is continuously mixed from batch concentrate and tap water by proportioning pumps located within the bowels of the dialysis machine or as a separate central delivery sys-

tem. The brisk countercurrent flows of blood and dialysate maximize diffusion opportunities. These innovations have allowed vastly greater clearance efficiency and predictability, with total environmental control over the purity, temperature, and chemical composition of the dialysate.

The Brescia-Cimino fistula, the polysulfone "high flux" hemodialyzers, and dialysis machines featuring computerized governance of dialysate composition and fluid removal rates have brought hemodialysis to its present state of service.

Membrane materials have also evolved. For over 30 years, dialysis membranes have been made from a cellulose derivative called cuprophane. Cuprophane kidneys remain in common use but they are reactive to blood, activating the complement system and promoting pulmonary vascular leukostasis. In an attempt to diminish reactivity and further improve clearance efficiency, advanced synthetic membranes have been introduced. These include polymethylmethacrylate, polyacrylonitrile, and most recently an exceedingly inert and sturdy polysulfone membrane. Because of polysulfone's strength, it can be given larger pores without compromising textile integrity. Thus, in nearly the same size cartridge, the polysulfone hollow fiber kidney more than doubles small solute clearance while greatly increasing middle and large molecular weight solute clearances, which are comparatively very low with the conventional cuprophane kidneys. However, these dialyzers require a new generation of dialysis machine capable of precise volumetric

control of the rate of fluid removal during hemodialysis, for the new polysulfone dialyzers are capable of stripping blood of its water at a rate in excess of 250 cc per minute. Left ungoverned, the patient could experience a complete vascular collapse in minutes. Yet, with electronically governed volumetric filtration control machines and polysulfone hollow fiber kidneys, "high efficiency" and "high flux" hemodialysis is now routinely accomplished with 2-3 hour dialysis times while providing superior clearances of small and large solutes alike.

The Brescia-Cimino fistula, the polysulfone "high flux" hemodialyzers, and dialysis machines featuring computerized governance of dialysate composition and fluid removal rates have brought hemodialysis to its present state of service. Yet, recognizing and defining what constitutes "adequate dialysis" for each patient has been elusive and the technologic capability for shorter dialysis times has heightened the tension.⁷ Nephrologists have long agreed that there is no one index which can serve as a routine indicator of dialysis adequacy. Overall patient well-being, discerned from a thorough clinical assessment, is probably not enough, for the problems of underdialysis most often smolder subclinically and become overt in late stages. Simply following blood chemistries has not been adequate either.⁸ While all nephrologists gauge dialysis times according to patient well-being and blood chemistry values, there has been a need to more precisely define what constitutes sufficient dialysis, particularly in our present era of crowded dialysis units with congressionally constrained budgets and shorter dialysis times. A recently developed index employs a computation of actual urea clearance dur-

ing dialysis, which is then factored for urea appearance from dietary protein intake and catabolism. Termed Kt/V , the index incorporates the membrane diffusability of urea, dialysis time, the patient's body water volume, and the blood flow rate through the dialyzer. Values derived from this index correlate with patient well-being, hospitalizations, cardiovascular problems, and survival.⁷ The nephrologist then orders the dialysis time, blood flow rate, and dialyzer size to achieve a Kt/V exceeding 1.0 to 1.2. With this index, hemodialysis has become properly "prescriptive" whereby each patient is dialyzed to achieve a urea clearance appropriate to their protein intake, metabolism, and body size. While this concept has gained wide acceptance and routine implementation, it is recognized that urea clearance is only one measure of dialysis adequacy, and may falsely represent dialysis adequacy since urea is the easiest solute to remove via conventional hemodialysis.⁹ Nevertheless, this index represents a conceptual advance that maximizes the benefits of the newer technology and allows individually tailored and prescriptive therapy.

Emergence of Continuous Ambulatory Peritoneal Dialysis

While hemodialysis units grew with the fruits of significant technological innovations, a new method of peritoneal dialysis emerged as a viable and sometimes preferred alternative to the hemodialysis modality.

Intermittent peritoneal dialysis was first employed in the successful treatment of uremic patients in the 1940s by Frank, Fine, and Seligman of Boston who were actually charged by the federal government to develop a method of support for the war-wounded person with renal failure. While

these physicians achieved success with intermittent peritoneal dialysis, its broad application was stalled by the extraordinary amount of time and effort required to achieve sufficient dialysis clearances (eg, 40-60 hours per week, given in either 3 separate 12-16 hour sessions, or as one marathon session). Furthermore, each session of peritoneal dialysis required a new peritoneal penetration with a temporary access catheter. Needless to say, repeated abdominal punctures were increasingly hazardous, and major intra-abdominal trauma and infection were not uncommon.¹⁰ To address these problems, Tenckhoff introduced a modification of the rubber peritoneal catheter in 1964, adding Dacron cuffs to the mid-section of the catheter that he fashioned out of sialastic.¹¹ These Dacron cuffs are sutured in the abdominal wall, sealing the catheter tunnel and creating a fibrous barrier between the peritoneum and the catheter exit site. With this innovation, the dialysis catheter could be left in place, and repeated dialyses could be carried out with the same catheter. Even with the Tenckhoff modification and a sharp decline in complication rates, peritoneal dialysis remained an unpopular alternative to hemodialysis, largely because of its tediousness and poor patient rehabilitation rate.

Then in 1976, Popovich and Moncrief from Austin, Texas conceived of performing continuous peritoneal dialysis with long dwell periods and along with Karl Nolph of Missouri launched a trial of "continuous ambulatory peritoneal dialysis" (CAPD).¹² Rather than repeated rapid infusions with short dwells of dialysate performed while the patient was recumbent in bed, CAPD was intended to achieve continuous dialysis with minimal lifestyle in-

terruption. It was proposed that if dialysate were left to dwell in the abdomen for 4-6 hours, urea concentration in the solution would become equal to that in the blood. As well, other solutes would equilibrate at a rate determined by their size and concentration gradient. If the fluid were to dwell for 3-4 hours and then be quickly exchanged 5-6 times per day, it was thought that adequate solute removal would ultimately be achieved provided dialysis was uninterrupted, 7 days a week. Indeed, this was the case. Moncrief, Popovich, and Nolph introduced a method that used a two liter bottle of peritoneal dialysate, which was instilled into the abdominal cavity through the Tenckhoff catheter. This fluid was then allowed to equilibrate for about 6 hours, then outflowed, and then fresh dialysate was immediately instilled. The exchange of dialysate was performed typically 4 times per day with even spacing, and dialysate continuously dwelled between these exchanges, including overnight.

It was immediately apparent that CAPD could achieve its intent: adequate dialysis with minimal lifestyle interruption, but problems existed. For one, infection was frequent, as the system was not entirely closed and bacteria had ample opportunity to gain entrance into the abdomen. Secondly, the glass bottles were an encumbrance, being difficult to transport and awkward to dispose. Within 4 years, however, as industry became involved, specially engineered tubing connectors and flexible collapsible bags were introduced, and CAPD gained wider interest and acceptance.

Since 1980, advantages of CAPD have become apparent and medical indications for selection of CAPD over hemodialysis have evolved.¹² For example, potas-

sium build-up between hemodialyses often threatens the inter-

... patients with hypertensive or congestive cardiomyopathy are often better served with continuous ambulatory peritoneal dialysis than with hemodialysis.

mittently dialyzed patient, whereas CAPD provides continuous clearance. The same can be said of salt and water build-up which threatens some patients with pulmonary congestion and untoward hypertension before each hemodialysis session. Thus, patients with hypertensive or congestive cardiomyopathy are often better served with CAPD than with hemodialysis. CAPD has also evolved as a preferred modality for the diabetic patient. Heparin, which is necessary for hemodialysis, is avoided which may protect the retina; hypertension is often better controlled owing to more constant fluid control; and insulin is administered directly into the dialysate, which provides direct glycemic coverage as glucose is absorbed from the dialysate. CAPD is also preferred for the very young or the very old who often cannot tolerate the vigor and abruptness of hemodialysis treatment. Patients with severe coronary disease and unstable angina seem to fare better with CAPD than hemodialysis, once again because the cardiac stress of hemodialysis is avoided. And, of course, CAPD is an alternative for the patient with vascular access exhaustion.

Many patients select CAPD for personal reasons: they can dialyze at home and remain independent from a rigid in-center hemodialysis schedule; they can travel easily and frequently, can work on a daily basis without

much interruption and can even perform exchanges at work; patients on CAPD also eat more liberally, because dialysis is continuous and there is not a peak predialysis build-up of solutes and fluid. Many people find they simply feel better compared to how they felt on hemodialysis. However, the patient who is successful with CAPD must be highly motivated, self-reliant, and/or have a supportive, reliable family. Compliance must not falter and technique must be precise so as to assure sterility. Despite continuous modifications in technique, bacterial peritonitis remains a concern. The national average is one episode of peritonitis per patient every 8-9 months.¹² These infections are usually minor, and easily treated with intraperitoneal antibiotics, which patients are taught how to use, and most often do not require hospitalization. The usual pathogens are skin flora, not intestinal bacilli, indicating infection by contamination rather than from a bowel source.

Other problems exist. Some patients "burn-out" from the daily routine. Hyperlipidemia can evolve from the large carbohydrate load which may accelerate atherosclerosis. Large proteins as well as amino acids are dialyzed away, so protein malnutrition is a threat and concern. For this reason, patients on CAPD are prescribed a diet high in protein (1.2 – 1.5 gm/kg day) yet low in fat which for many is a difficult feat to accomplish. Body image often changes due to the frontal presence of the catheter and abdominal distension, and mechanical problems do arise, such as hernias, low back pain, and pleural effusion, so some patients may drop CAPD after trying it for only a few months.

Nevertheless, CAPD is a significant recent advance that presents a viable and often preferred

alternative to hemodialysis. It is equivalent in effectiveness, less expensive than in-center hemodialysis, easily done, and increas-

... the patient who is successful with continuous ambulatory peritoneal dialysis must be highly motivated, self-reliant, and/or have a supportive, reliable family.

ingly utilized. Presently in the United States, approximately 20,000 patients dialyze with CAPD, representing 15–20% of the dialysis population and accrual is steadily rising. Whether CAPD is capable of providing renal replacement therapy for many consecutive years (10–25 years), as hemodialysis has proven it can, remains an open question. Active research is ongoing. The consensus to date is that CAPD is a very positive innovation and is here to stay.

Aluminum Problems and Erythropoietin

The aforementioned advances in dialytic management have had substantial positive impact on the patient with renal failure, providing greater efficiency, effectiveness, tolerability, and availability of dialytic therapy with enhanced rehabilitative opportunity. In addition, two non-dialytic aspects of the care of these patients have had substantial impact and merit special discussion: (1) the realization that oft-prescribed aluminum in antacids is biologically toxic in these patients, and (2) the introduction of erythropoietin as a replacement hormone used for the correction of the anemia which universally accompanies renal failure.

Aluminum. Long held to be biologically inert and of no clinical

consequence, compelling evidence now exists that aluminum is a major factor leading to encephalopathic brain damage and bone mineralization arrest in the renal failure patient. The initial correlation was suggested by Alfrey, who documented a gross elevation of the brain content of aluminum in dialysis patients dying with a peculiar, rapidly progressive encephalopathy.¹³ The aluminum content of brain gray matter from his patients dying with encephalopathy was 4-fold greater than that of hemodialyzed patients dying for other reasons, 6-fold greater than non-dialyzed uremic patients, and 12-fold greater than control tissues. Similar "outbreaks" of progressive dialysis encephalopathy have been associated with high tissue levels of aluminum; and laboratory models have confirmed aluminum CNS toxicity. In humans, manifestations include dysarthria and apraxia, personality changes, dementia, psychosis, myoclonus, seizures, and progressive stupor. Death is usual.¹⁴

Progressive neurologic toxicity is not the only consequence of aluminum overload in these patients. Aluminum is concentrated as well in bone and is associated with progressive osteomalacia that is resistant to vitamin D therapy. Using electron probe techniques and tetracycline labelling, aluminum has been found in large quantities along the bone mineralization front in many patients with uremic osteodystrophy. Its association with progressive bone disease is no longer questioned, and aluminum-associated renal osteodystrophy is now a widely recognized problem, causing significant morbidity along with the osteitis fibrosa lesion of hyperparathyroidism and the pure osteomalacia of 1,25 vitamin D₃ deficiency. In some dialysis centers, aluminum-associated osteodys-

trophy accounts for up to 30-40% of all bone disease on the unit.¹⁵

... compelling evidence now exists that aluminum is a major factor leading to encephalopathic brain damage and bone mineralization arrest in the renal failure patient.

Aluminum can accrue in the tissues of dialysis patients from two sources: the dialysis water and from oral ingestion of aluminum-based phosphate binders. Since water treatment plants often add aluminum sulfate as a flocculating agent, community water supplies may be high in aluminum. The individual with healthy kidneys easily excretes ingested aluminum, but for the patient with renal failure there is no exit. Aluminum in dialysis water easily transfers into the blood down its concentration gradient. There being no exit, aluminum is bound by plasma proteins and taken up by tissues. Significant accumulations can occur in a matter of months to years. Of equal concern is the documentation that a substantial amount of aluminum is absorbed following the oral intake of aluminum-based phosphate binders. In fact, it has been shown that total body content of aluminum can increase significantly over time solely from aluminum antacids in non-dialyzing patients with renal insufficiency.¹⁶

As patients are surviving for many years with renal replacement therapy, these insidious threats from aluminum have become major concerns. To remove the possibility of aluminum infusion during dialysis, it is now standard that all dialysis facilities be served with water purification units. Usually, this is accom-

plished by reverse osmosis units that treat the incoming tap water prior to being proportioned with the dialysate concentrate solution. Water receiving such treatment is rendered mineral-free. Aluminum ingestion from phosphate binders, however, remains a large concern. To mitigate this, many nephrologists now prescribe calcium carbonate as the first choice phosphate binder, which is generally effective but not universally so.¹⁷ Aluminum hydroxide or aluminum carbonate still must occasionally be employed to control the plasma phosphate. There is an unconfirmed suggestion that calcium acetate may have more effect due to its greater ionization in the alkaline environment of the small intestine.¹⁸ Most nephrologists are now aware of the possibility of insidious aluminum overload and include plasma aluminum in routine lab testing. However, this is not adequate and patients have to be tested by a deferoxamine chelation challenge, which more accurately detects tissue burden of aluminum.¹⁹

Erythropoietin. The introduction and growing use of human recombinant erythropoietin (Epo) probably merits distinction as the single recent advance with the greatest impact for the patient with renal failure. Anemia of chronic renal insufficiency was recognized by Richard Bright,¹ though mechanisms were unknown. For three decades now, it has been known that patients with renal failure are deficient in erythropoietin production, which is thought to center normally in the capillary endothelial cells of the renal cortex and/or in a set of differentiated peritubular interstitial cells. Scarred kidneys produce little erythropoietin. While the anemia of renal disease is primarily due to erythron hypoproliferation owing to erythropoietin

deficiency, other factors such as uremic suppression of the marrow, protein malnutrition, and shortened red blood cell survival are also operative. Nevertheless, regular administration of recombinant human erythropoietin can stimulate erythropoiesis sufficiently to normalize the hematocrit in over 95% of patients, provided adequate iron is available for erythropoiesis, the marrow is not fibrosed or imbued with aluminum, and adequate doses are given.²⁰

The erythropoietic response from recombinant human erythropoietin is dose-dependent, as would be expected for any hormone replacement therapy.²⁰ For example, doses of 40 units/kg given 3 times a week will raise the hematocrit to a target level of 35 by 3 months in only 30% of hemodialysis patients; 75% will reach the target hematocrit of 35 with 80 units/kg thrice weekly, and 93% will reach a hematocrit of 35 with 120 units/kg. Hemodialysis patients do not seem to respond to doses less than 20 units/kg. Most physicians feel that the target hematocrit should be 33-36% and Epo is dosed accordingly. When hematocrit nears 36%, Epo dosages are titrated to maintain the hematocrit without decline and to prevent further undesired elevations. Available for general use for only one year, the average dose nationwide is 40-75 units/kg 2-3 times weekly.²⁰

Correction of the anemia in dialysis patients has dramatic benefits, and marked changes in patient well-being are common. The need for transfusions is virtually eliminated as the hematocrit rises, and the savings in the consumption of banked blood are large. From the Epo-stimulated higher hematocrits, better tissue oxygenation ensues, resulting in measurable improvements in tissue functioning. For example, car-

diac output decreases from elevated to normal with concomitant reductions in left ventricular diastolic diameters. Wall tension diminishes and regional myocardial perfusion improves. Exercise capacity as measured by maximal oxygen utilization improves as does overall stamina and endurance. Cognitive functions improve, particularly memory, attention span, and neuropsychological parameters. Attitudes improve and sleep disorders disappear. Patient surveys indicate that sexual desire and potency are returning, and for some, even fertility returns. In summary, patients receiving Epo are experiencing subjective improvements and exhibiting physiologic reversal of many derangements we have come to recognize as part of the "uremic" condition.²⁰

Three concerns have come to light. Iron deficiency can quickly evolve as available iron is utilized. Most patients require iron supplementation and many are requiring parenteral iron therapy. Iron depletion thwarts Epo response, resulting in drug waste if the problem is not addressed. In many patients, blood pressure is noted to rise as hematocrit rises. Several mechanisms have been suggested, including a rise in blood volume, increased blood viscosity, augmented salt intake (from improved appetite), reduced dialyzer clearance of sodium and water, and an increase in peripheral vascular resistance. There may be some contribution from all these mechanisms, but the most consistent observation has been a rise in peripheral resistance. It is thought that chronic anemia induces hypoxic peripheral vasodilation; as anemia is corrected, reversal would occur, leaving the patient comparatively vasoconstricted. In some cases, accelerated or malignant hypertension has occurred as hema-

tocrits rose quickly from use of high doses of Epo. Therefore, there has been a trend to initiate therapy with doses less than 100 units/kg. A third concern is increased coagulability. Platelet counts rise slightly and platelet functions improve, but increased blood viscosity probably also contributes. Increased clotting of arteriovenous grafts and fistulae has been reported, and a concern has been voiced that we may actually see an increase of thrombotic coronary and cardiovascular events.²⁰

Nonetheless, the clinical experience with Epo has been overwhelmingly positive, albeit brief. The initial hope with Epo therapy was that use of transfusions would diminish and patients would simply feel better. Much more has happened. The physiologic changes following correction of the anemia are profound and not yet fully realized or understood. Certainly, it is becoming clear that some of the disability and morbidity of end-stage renal disease is anemic and not exclusively uremic. We can expect to hear more about Epo as its usage grows and patients are maintained on it longer.²¹

Advances in Renal Transplantation

This brief essay about advances in the care of the renal patient cannot be concluded without mention of two advances in the field of renal transplantation: use of cyclosporine A as maintenance anti-rejection therapy, and use of monoclonal antibodies as induction anti-rejection therapy.

Renal transplantation had its successful beginnings in Boston in 1954 with the successful transplantation of a kidney between identical twins. Minimal anti-rejection therapy was required, and the graft survived. Despite initial enthusiasm, renal transplanta-

tion grew only hesitantly because most patients did not have a twin donor and the problems of graft rejection were large. Cadaver transplantations were attempted and various anti-rejection regimens were tried, but the protocol finally achieving widespread acceptance utilized azathioprine 2-3 mg/kg/day and prednisone. However, problems abounded, as graft acceptance remained low — 55% graft survival at one year with a steady decline thereafter for cadaver transplantations — and was only modestly better for living related donor transplantation — 75-80% graft survival at one year and 60-65% at 5 years. And patient survival was not certain. Through 1974, nearly 25% of cadaver kidney recipients would die during the first year following transplantation, this high rate owing to the broad immunosuppression and marrow toxicity of azathioprine and the then common practice of employing very high dose corticosteroids for each rejection episode.²² In those times, the certainty of hazard and the uncertainty of graft survival gave pause to nephrologists and patients alike when the subject of transplantation was brought to discussion. In the early 1980s, use of anti-lymphocyte globulin moved average cadaver graft survival up toward 75% at one year, but serum sickness reactions and greater infectious complications were constant concerns.²²

Then, both cyclosporin A and monoclonal antibodies were introduced into the anti-rejection armamentarium and a quantum leap in graft survival statistics resulted.^{23, 24} Both of these agents have selective immunosuppressive properties as opposed to azathioprine, which is comparatively non-selective. Cyclosporin A, a peptide derived from a fungus, causes almost total inhibition of T lymphocyte proliferative re-

sponses while exerting little direct effect on B lymphocytes, neutrophils, or monocytes. OKT3, the monoclonal antibody currently in routine use, selectively inhibits only the T3 subset of T lymphocytes, which generally serve to recognize foreign antigens and initiate an immune response. The selectivity seems beneficial in two regards: myeloid cells are unaffected so host defenses are not as impaired as with azathioprine, and tissue rejection responses seem more effectively held at bay because of the focused lymphocytic interference. At present, OKT3 is widely employed as prophylactic anti-rejection therapy in the first 2-3 weeks of transplantation. If anti-OKT3 antibodies do not form, it may be reapplied weeks later for therapy of an acute rejection episode. Cyclosporin A is typically prescribed at the time of transplantation and carried as a maintenance immunosuppressive drug, always in combination with prednisone and at times in combination with azathioprine. With either of these agents, graft rejection episodes are less frequent with graft survival approaching 90% at one year; and because of less rejection morbidity, lower accumulative doses of corticosteroid, limited myelotoxicity, and stronger host defenses, patient survival is exceeding 94%.²⁵

Cyclosporin A does have its own toxicity, however. It causes hypertension, has been associated with emergence of lymphomas, can cause a peripheral neuropathy, is often hepatotoxic, and most worrisome of all, is predictably nephrotoxic. There appears to be two types of nephrotoxicity: an acute toxicity which reverses with dose reduction, and a chronic form which is associated with histologic changes and progressive nephrosclerosis.

Notwithstanding these prob-

lems, which are generally manageable, cyclosporin A has propelled not only renal transplantation but all organ transplantation into a new era. Varied protocols continue to be tested with cyclosporin A, monoclonal antibodies, corticosteroids, and azathioprine. Toxicity is declining as we learn more about the drugs, and graft survival is breeching 90%. It is clear that the early tentativeness of transplantation is waning. With cyclosporin A and OKT3, waiting lists are growing longer despite rising rates of transplantation. Nephrologists are now referring a majority of patients under the age of 55 for transplant consideration, and more patients spontaneously express a desire to have a go at what truly seems to be the ultimate renal replacement therapy — a new kidney.

References

- 1 Bright R, Cases and Observations Illustrative of Renal Disease Accompanied with Secretion of Albuminous Urine *Guys Hosp Rep* 1:388, 1836.
- 2 Drukker W, Hemodialysis: A Historical Review Chapter 3, pp. 20-86 in *Replacement of Renal Function by Dialysis*, Ed. Maher JF. Kluwer Academic Publishers, Boston; 3rd Ed, 1989.
- 3 Quinton W, Dillard D, Scribner BH, Cannulation of Blood Vessels for Prolonged Hemodialysis. *Trans Am Soc Artif Intern Organs* 6:104-113, 1960.
- 4 Brescia MJ, Cimino JE, Appel K, Hurwich BJ, Chronic Hemodialysis Using Venipuncture and a Surgically Created Arteriovenous Fistula. *N Engl J Med* 275:1089-1092, 1966.
- 5 Gutman RA, Stead WW, Robinson RR, Physical Activity and Employment Status of Patients on Maintenance Hemodialysis. *N Engl J Med* 304:309-313, 1981.
- 6 Lundin AP, Prolonged Survival on Hemodialysis, Chapter 56, pp. 1133-1140 in *Replacement of Renal Function by Dialysis*, Ed. Maher JF. Kluwer Academic Publishers, Boston; 3rd Ed, 1989.
- 7 Hakim RM, Assessing the Adequacy of Dialysis. *Kidney Int* 37:822-832, 1990.
- 8 Teschan PE, Ginn HE, Bourne JR, Ward JW, Hamel B, Nunnally JC, Musso M, Vaughn WK, Quantitative Indices of Clinical Uremia. *Kidney Int* 15:676-697.
- 9 Levin NW, Gotch FA, Daugirdas JT, Teschan PE, Collins AJ, Keshaviah P, What is the Role of KT/V Urea in Chronic Dialysis? *Sem Dialysis* 3:73-80, 1990.
- 10 Drukker W, Peritoneal Dialysis: A Historical

- Review. Chapter 22, pp. 476-509 in *Replacement of Renal Function by Dialysis*, Ed. Maher JF, Kluwer Academic Publishers, Boston; 3rd Ed, 1989.
- ¹¹ Tenckhoff H, Schechter H, A Bacteriologically Safe Peritoneal Access Device. *Trans Am Soc Artif Organs* 14:181-187, 1968.
 - ¹² Nolph K, Continuous Ambulatory Peritoneal Dialysis. *N Engl J Med* 318:1595-1600, 1988.
 - ¹³ Alfrey AC, LeGendre GR, Kaehny WD, The Dialysis Encephalopathy Syndrome — Possible Aluminum Intoxication. *N Engl J Med* 294:184-188, 1976.
 - ¹⁴ Fraser CL, Arief Al, Nervous System Complications of Uremia. *Ann Int Med* 109:143-153, 1988.
 - ¹⁵ Mallucha H, Faugere MC, Renal Bone Disease 1990: An Unmet Challenge for the Nephrologist. *Kidney Int* 38:193-211, 1990.
 - ¹⁶ Kaehny WD, Hegg AP, Alfrey AC, Gastrointestinal Absorption of Aluminum from Aluminum-Containing Antacids. *N Engl J Med* 296:1389-1390, 1977.
 - ¹⁷ Fournier A, Moriniere P, Sebert JL, Okhissi H, Atik A, Leflon P, Renaud H, Gueris J, Gregoire I, Idrissi A, Garabedian M, Calcium Carbonate: An Aluminum-free Agent for Control of Hyperphosphatemia, Hypocalcemia, and Hyperparathyroidism in Uremia. *Kidney Int* 29:5114-5119, 1986.
 - ¹⁸ Mai ML, Emmett M, Sheikh MS, SantaAna CA, Schiller L, Fordtran JS, Calcium Acetate: An Effective Phosphorus Binder in Patients with Renal Failure. *Kidney Int* 36:690-695, 1989.
 - ¹⁹ Milliner DS, Nebeker HG, OTT SM, Andress DL, Sherrard DJ, Alfrey AC, Slatapolsky E, Coburn JW, Use of the Deferoxamine Infusion Test in the Diagnosis of Aluminum-related Osteomalacia. *Ann Int Med* 101:775-780, 1984.
 - ²⁰ Eschbach JW, Haley NR, Adamson JW, New Insights into the Treatment of the Anemia of Chronic Renal Failure with Erythropoietin. *Sem Dialysis* 3:112-121, 1990.
 - ²¹ Ad Hoc Committee for the National Kidney Foundation, Fisher JW (chairman). Statement on the Clinical Use of Recombinant Erythropoietin in Anemia of End Stage Renal Disease, *Am J Kid Dis* 14:163-167, 1989.
 - ²² Strom TS. The Improving Ability of Renal Transplantation in the Management of End-Stage Renal Disease. *Am J Med* 73:105-124, 1982.
 - ²³ Canadian Multicenter Transplant Study Group: A Randomized Clinical Trial of Cyclosporine in Cadaveric Renal Transplantation, *N Engl J Med* 309:809-815, 1983.
 - ²⁴ Ortho Multicenter Transplant Study Group: A Randomized Clinical Trial of OKT3 Monoclonal Antibody for Acute Rejection of Cadaveric Renal Transplants, *N Engl J Med* 313:337-342, 1985.
 - ²⁵ Glasscock RJ. Outcome of Renal Transplantation, Chapter 89, pp. 1551-1562 in Massry SG, Glasscock RJ, *Textbook of Nephrology*, 2nd ed., Williams and Wilkins, Baltimore; 1989.

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Therapy-related adverse reactions are uncommon. Those reported include:

- Hypersensitivity reactions have been reported in about 1.5% of patients and include morbilliform eruptions (1 in 100), Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions have been reported with the use of Ceclor. These are characterized by findings of erythema multiforme, rashes, and other skin manifestations accompanied by arthritis/arthralgia, with or without fever, and differ from classic serum sickness in that there is infrequently associated lymphadenopathy and proteinuria, no circulating immune complexes, and no evidence to date of sequelae of the reaction. While further investigation is ongoing, serum-sickness-like reactions appear to be due to hypersensitivity and more often occur during or following a second (or subsequent) course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults with an overall occurrence ranging from 1 in 200 (0.5%) in one focused trial to 2 in 8,346 (0.024%) in overall clinical trials (with an incidence in children in clinical trials of 0.055%) to 1 in 38,000 (0.003%) in spontaneous event reports. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy; occasionally these reactions have resulted in hospitalization, usually of short duration (median hospitalization = two to three days, based on postmarketing surveillance studies). In those requiring hospitalization, the symptoms have ranged from mild to severe at the time of admission with more of the severe reactions occurring in children. Antihistamines and glucocorticoids appear to enhance resolution of the signs and symptoms. No serious sequelae have been reported.

- Stevens-Johnson syndrome, toxic epidermal necrolysis,

and anaphylaxis have been reported rarely. Anaphylaxis may be more common in patients with a history of penicillin allergy.

- Gastrointestinal (mostly diarrhea): 2.5%
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.

- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1% and, rarely, thrombocytopenia and reversible interstitial nephritis.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient lymphocytosis, leukopenia, and, rarely, hemolytic anemia and reversible neutropenia.
- Rare reports of increased prothrombin time with or without clinical bleeding in patients receiving Ceclor and Coumadin concomitantly.
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and ClinTest[®] tablets but not with Tes-Tape[®] (glucose enzymatic test strip, Lilly).

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Recent Advances in Infectious Diseases

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Human papillomavirus may be the most common sexually transmitted disease in the United States.

As the decade of the 1980s comes to a close, the AIDS epidemic continues to dominate the clinical and research efforts of infectious disease physicians. Despite considerable advances in the understanding of the human immunodeficiency virus and its immunopathogenic mechanisms, eradication of the organism and the development of an effective vaccine continues to elude medical science. The AIDS epidemic has become a human tragedy of immense proportions and it will continue to be the most pressing and challenging infectious disease priority in the United States during the 1990s.

In contrast to the disappointingly slow progress in AIDS research, important advances in the microbiology and treatment of a variety of other infectious dis-

eases have occurred recently. A number of previously unrecognized, human pathogens have been identified within the last few years. The recognition of *Helicobacter pylori* as a cause of upper gastrointestinal inflammation, *Chlamydia pneumoniae* as a cause of respiratory tract infection, and *Ehrlichia canis* as a common rickettsial infection are examples of important recent discoveries.

In this review, we intend to briefly summarize some of the most significant recent advances of clinical relevance in infectious diseases. Important discoveries in clinical microbiology are described in Table 1. New therapeutic options in the management of infectious diseases are reviewed in Table 2.

HIV and the AIDS Epidemic

Some interesting national trends are emerging from the AIDS statistics that are worthy of note. While the incidence of new AIDS cases is increasing in virtually all major high risk groups (35,328 cases in 1989 in US), the incidence of transfusion-acquired or clotting factor-acquired AIDS appears to have leveled off and may even be decreasing.¹ This is undoubtedly related to the universal

screening of blood transfusion products in the United States. The incidence of new AIDS cases in gay men appears to be slowing slightly as well. This may be related to the success of educational programs and AZT treatment which slows the immunosuppression related to HIV infection. Improved preventive measures such as aerosolized pentamidine and prophylaxis against fungal infections may also be having an impact on AIDS statistics.

The most troubling findings include the progressive increase of AIDS in intravenous drug users and heterosexual partners of high risk groups.² Perinatally transmitted HIV infection is also increas-

ABBREVIATIONS USED:

AIDS: acquired immunodeficiency syndrome

AZT: zidovudine

CSF: cerebrospinal fluid

ddC: 2' 3' dideoxycytidine

ddl: 2' 3' dideoxyinosine

DNA: deoxyribonucleic acid

HIV: human immunodeficiency virus

HPV: human papillomavirus

LPS: lipopolysaccharide

RMSF: rocky mountain spotted fever

TNF: tumor necrosis factor

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ing. AIDS is now observed with greater frequency in smaller cities throughout the United States.¹

Zidovudine (AZT) has clearly had an impact on the AIDS epidemic and has prolonged the survival of HIV infected patients. Recent data demonstrating the utility of lower doses of AZT (500 mg/day) is welcome news owing to its decreased cost and improved compliance coupled with decreased toxicity.^{3,4} Recent observations of AZT resistance in patients with HIV is worrisome.⁵ While the clinical consequences of AZT resistance is not yet known, this provides increased impetus for the development of new antiretroviral agents.

Recent observations of AZT resistance in patients with HIV is worrisome.

The importance of preventive care and provision of early treatment for opportunistic infections has improved the outlook for HIV infected patients. HIV infection may gradually become a chronic, manageable illness rather than a rapidly fatal disease as our knowledge of its natural history improves.^{1,6} The subject of HIV and its impact on health care in Rhode Island and the rest of the United States has recently been reviewed in detail in the *Rhode Island Medical Journal*.⁷

Ehrlichiosis

The *Ehrlichia* species are obligate intracellular bacteria that are grouped with the *Rickettsiaceae*. The pathogenic nature of these tick-transmitted, rickettsial organisms was first appreciated during the Vietnam War when military sentry dogs became infected with *Ehrlichia canis*. Dogs developed a highly fatal hemorrhagic disease named tropical canine pancytopenia.⁸ Human ehrlichiosis was initially described in the

Table 1. Recent Discoveries in Clinical Microbiology

Organism	Disease Association	Comments
<i>Ehrlichia canis</i>	Rickettsial disease with fever, myalgia, cytopenias	Probably tick transmitted. Found in Southeast and Central US.
<i>Helicobacter pylori</i> (Campylobacter pylori)	Type B gastritis, peptic ulcer	Antibiotics may prevent recurrences in ulcer disease
<i>Chlamydia pneumoniae</i> (TWAR)	Upper and lower respiratory infection	Common in children and young adults
Human papillomavirus type 16 and 18	Cervical dysplasia and carcinoma	An important, subclinical sexually transmitted disease
Parvovirus B19	Fifth disease, bone marrow failure in immunocompromised patients	Transient aplasia in normal hosts, persistent aplasia in immunosuppressed
Hepatitis C (Non-A, Non-B Hepatitis)	Post-transfusion hepatitis	Serologic test now available to protect blood supply
Hepatitis E	Enterically-transmitted hepatitis	Similar to hepatitis A but a distinct, new virus
Cat-scratch disease bacillus	Cat scratch disease	Organism successfully cultured, potentially treatable
Human Herpes virus 6 (HH6)	Roseola	Ubiquitous virus, probable cause of this childhood exanthem

US in 1986. An Arkansas man developed fever, myalgias and pancytopenia following the removal of a tick. Intracytoplasmic inclusion bodies were found in his leukocytes. Serologic studies confirmed infection with *E. canis* and he was successfully treated.^{9,10}

The diagnosis (of ehrlichiosis) is confirmed serologically and treatment consists of tetracycline or chloramphenicol.

Subsequently cases have been found in southern and central United States. Ehrlichiosis is most common in young men during the summer months in rural areas. Three-quarters of the patients report tick exposure prior to onset of symptoms implicating a tick vector in most cases. Clinical manifestations are nonspecific

and are similar to those seen in Rocky Mountain Spotted Fever (RMSF). In contrast to RMSF, only about 20% of patients have rash and less than 5% have rash on the palms or soles. Leukopenia, anemia, thrombocytopenia, and elevated liver-associated enzymes also are distinguishing characteristics of ehrlichiosis.^{10,11} Recent investigations¹² suggest that ehrlichiosis is more common than RMSF in many regions of the Southeast. The diagnosis is confirmed serologically and treatment consists of tetracycline or chloramphenicol.

Helicobacter Pylori

Helicobacter pylori was first isolated from gastric samples in 1982.¹³ Increasing evidence supports the pathogenic role of *H. pylori* in gastric inflammation and peptic ulcer disease. The organism is a motile, curved, gram-negative rod which produces

Table 2. Recent Advances in Preventing Treatment of Infectious Diseases

Agent	Indications	Comments
Dideoxyinosine (ddI)	HIV	May be useful in place of or in addition to AZT
Dideoxycytidine (ddC)	HIV	May be useful in place of or in addition to AZT
Fluconazole	Cryptococcal and candidal infection	Orally absorbed, well tolerated, excellent CSF levels
Mefloquine	Malaria	Effective in resistant cases of falciparum malaria
Corticosteroids	Bacterial meningitis in children	Limited experience in adults
Anti-endotoxin monoclonal antibody	Septic shock	Neutralizes endotoxin effects
Anti-TNF monoclonal antibody	Septic shock	Neutralizes toxic effects of TNF produced in septic shock
Live attenuated oral typhoid vaccine	Prevention of typhoid fever	Well tolerated, highly protective

urease in large quantities. The urease produced by this organism may protect it from gastric acidity, yet cause injury to the gastric mucosa through the generation of ammonia. A variety of serologic, histologic, microbiologic data support the role of *H. pylori* in upper gastrointestinal inflammation (Table 3). Recent evidence implicating *H. pylori* in Type B antral gastritis include: (1) human volunteer studies with *H. pylori* resulting in chronic gastritis; (2) an animal model using gnotobiotic pigs reproduces chronic gastritis following inoculation with *H. pylori*; (3) treatment with bismuth salts, nitrofurantoin or amoxicillin eradicates the organism and results in improvement in the gastric inflammation. Moreover, serologic responses to *H. pylori* indicate a systemic response to the organism.¹⁴

The role of *H. pylori* as a cause of peptic ulcer disease is more speculative. Current evidence indicates that excess gastric acid induces gastric metaplasia of regions of duodenal mucosa. *H. pylori* then colonizes these sites

Eradication of *Helicobacter pylori* was associated with prolonged remission of peptic ulcer disease.

where the production of urease and a microbial cytotoxin produces injury and subsequent duodenal ulceration. Gastric acidity as well as infection with *H. pylori* may contribute to peptic ulceration.¹⁴ Two recent reports^{15, 16} support the contention that *H. pylori* contributes to the pathogenesis of peptic ulcer. Combination therapy with antacid regimens or H₂ blockers with antibiotics resulted in lower recurrence rates when compared to antacid therapy alone. Eradication of *H. pylori* was associated with prolonged remission of peptic ulcer disease. Failure to eradicate the organism may be a cause of persistent and recurrent peptic ulcer in this patient population. A greater understanding of the biology of this organism may provide new insights into the prevention and treatment of peptic ulcer disease and upper gastrointestinal inflammation.

Chlamydia pneumoniae

A previously unrecognized *Chlamydia psittaci*-like organism was first recognized as a cause of human respiratory infection in 1986. This organism, initially referred to as TWAR, has now been carefully analyzed and is known to be a third species in the genus *Chlamydia* and is currently known as *C. pneumoniae*.¹⁷ This is a primary human pathogen and is transmitted between humans without an animal reservoir. The organism is an obligate intracellular bacterial pathogen which grows within epithelial cells. A number of serologic tests have been developed which have been invaluable in the understanding of the pathogenesis and epidemiology of this organism.¹⁸

The clinical manifestations of *C. pneumoniae* are similar to *Mycoplasma pneumoniae*. The disease is most frequently recognized in older children and young adults and is associated with pharyngitis, bronchitis, hoarseness and prolonged lower respiratory symptoms. While most infections appear to be mild, severe infections may occur. Up to 10% of hospitalized patients with pneumonias from a variety of areas of North America have been shown to be caused by *Chlamydia pneumoniae*. *C. pneumoniae* infection may be distinguished clinically by its propensity to cause prolonged respiratory illness and frequent hoarseness.¹⁹

Serologic studies have demonstrated that this is a ubiquitous organism in nature. While less than 10% of patients under age ten have serologic evidence of *C. pneumoniae* infection, up to 50% of patients over age 20 have seropositivity to *C. pneumoniae*. This would indicate that the majority of infections occur during adolescence and that most older adults have already experienced this infection. Immunity appears

***Chlamydia pneumoniae* is most frequently recognized in older children and young adults and is associated with pharyngitis, bronchitis, hoarseness and prolonged lower respiratory symptoms.**

to be incomplete and reactivation may occur from this organism. Treatment consists of prolonged courses of high dose tetracycline or erythromycin.¹⁷

Human Papillomavirus

It has recently become apparent that the human papilloma viruses (HPV) are important genital pathogens.²⁰ There are greater than sixty types of human papilloma viruses (HPV) identified by DNA probes with greater than 20 types infecting the genital tract. HPV types 16-18 are associated with subclinical infection of the cervix and possess significant malignant potential. Types 6-11 have a tendency to produce exophytic condylomata around the external anogenital region and Type 11 is also associated with papillomatous laryngeal disease. HPV DNA has been found in cancerous cervical tissue where it is integrated into the cellular chromosomes thus implicating it as a cause of cervical cancer. Use of DNA probes has also revealed HPV nucleic acids in histologically normal tissue. Asymptomatic infection appears to be quite common. For this reason it is difficult to predict which lesions will progress or how rapidly HPV 16 and 18 infected cells will lead to cervical cancer. HPV probably induces cervical carcinoma with the help of other cofactors. Possible cofactors include acquired or inherited factors that affect immune competence.^{20, 21}

HPV may be the most common

sexually transmitted disease in the United States. There are many clinical manifestations including flat condylomata, condyloma acuminata and bowenoid papulosis. These infections are visible on genital tissues, with magnification, after application of 3-5% acetic acid. Pap smears may reveal cervical dysplasia which is indicative of HPV infection. Many patients have multicentric disease with simultaneous HPV infections at various levels of the genital tract.²⁰

Transmission of HPV infection is primarily via sexual contact. Vertical transmission has been implicated in development of juvenile laryngeal papillomatosis in affected children. It is possible that HPV may be transmitted by other means as well. To reduce transmission of genital HPV, clinicians should recommend condom use to patients with new sexual partners. Condom use is usually unnecessary with current monogamous partners since the current partner is likely to be infected already.²¹

Treatment is difficult since: (1) the virus may persist in adjacent, normal appearing tissue; (2) no specific antiviral medication is available; (3) local treatment results in high failure rates. Present therapy includes use of podophyllin, trichloroacetic acid, cryotherapy, electrocautery or laser surgery. Immunologic destruction of anogenital warts with intralesional interferon-alpha appears to be a promising new therapeutic approach as well.²²

Other Recent Discoveries in Clinical Microbiology

It has now become evident that the parvovirus B19, the cause of erythema infectiosum, also produces a number of other important clinical syndromes. The organism may cause transient aplastic crises as well as chronic

and severe, persistent anemia. Chronic anemia is much more common in immunocompromised patients and may be one of the many causes of severe anemia in AIDS patients.²³ Recent reports of successful treatment of B19-induced chronic anemia with intravenous gamma globulin dramatically illustrate the potential impact of this viral infection on the bone marrow.²⁴ Parvovirus B19 also appears to produce an arthropathy in many adults infected with this virus. The risk of transplacental infection with resultant fetal hydrops appears to be small but real.²⁵ The availability of improved diagnostic techniques, such as polymerase chain reaction technology, will provide an opportunity to more fully understand the epidemiology of this viral pathogen.

One of the major accomplishments of the 1980s was the characterization of the viral agent responsible for post-transfusion hepatitis.²⁶ Non-A non-B hepatitis is now known to be primarily related to a single RNA virus belonging to the togavirus family. This virus is now named hepatitis C and is the most common cause of post-transfusion hepatitis. A reliable serologic test has been developed to detect hepatitis C which should protect the nation's blood supply from this virus.²⁷ Recent clinical studies have also demonstrated the utility of alpha-interferon in controlling chronic hepatitis C virus infection.²⁸

The enterically transmitted non-A, non-B hepatitis agent is now known to differ from hepatitis C.²⁹ This virus has caused food and water-borne outbreaks in Asia and recently in South America.³⁰ The organism is similar to hepatitis A yet is serologically and virologically distinct. The virus is now named hepatitis E and its nature and ecology remain to be defined.²⁹

The infectious agent which causes cat-scratch disease has now been isolated and propagated in the laboratory. An animal model for cat-scratch disease now exists in armadillos. Cat-scratch disease is known to be caused by a thin, pleomorphic, gram negative bacterium. The organism, which has yet to be officially named, is aerobic and has been cultured on routine bacteriologic media.³¹ A serologic test has recently been developed which may aid in the diagnosis of this disease. The organism is susceptible *in vitro* to a variety of antimicrobial agents including third generation cephalosporins, aminoglycosides, extended spectrum penicillins, rifampin and quinolones. Recent reports of severe cat-scratch disease in immunocompromised patients and case reports of successful treatment with antibiotics has stimulated renewed interest in specific antimicrobial chemotherapy against this disease.^{32, 33}

The elusive agent which causes roseola may have recently been discovered. There is convincing serologic data to suggest that the human herpes virus Type VI (HH6) is, in fact, the viral cause of roseola. This common childhood exanthem, sometimes referred as exanthem subitum, is probably caused by this ubiquitous, recently discovered herpes virus.³⁴

Dideoxyinosine and Dideoxycytidine

The search for antiretroviral drugs in the treatment of HIV infection has resulted in the development of two, potentially useful, reverse transcriptase inhibitors.³⁵ 2' 3'-dideoxyinosine (ddI) is a purine dideoxynucleoside analogue that has *in vitro* activity against HIV in T cells and monocytes. Once inside the cell, ddI is metabolized to form the active compound di-

deoxyadenosine — 5'-triphosphate (ddA-TP). It preferentially inhibits HIV reverse transcriptase and suppresses HIV replication by blocking viral DNA synthesis. The intracellular half-life of the active compound is 12 hours allowing for once daily dosing. Side effects are painful peripheral neuropathy and pancreatitis that are probably both dose-related. Dose-related hyperuricemia is described which probably reflects metabolic degradation of ddI and is usually asymptomatic.^{35, 36}

2', 3'-dideoxycytidine (ddC) is a pyrimidine analogue that is inactive until it is metabolized to the 5' triphosphate form. The active form acts as a substrate for HIV-1 reverse transcriptase with subsequent inhibition of viral DNA. Its elimination half life is 1.2 hours and is excreted by the kidneys. This compound also partially penetrates the CSF following oral absorption. Decreased levels of HIV-associated P24 antigen, slight increases of CD4 cells (helper T lymphocytes) and some increase in antigen induced T cell proliferation *in vitro* have been noted following ddC therapy in AIDS patients. Side effects include maculovesicular rash, aphthous oral ulcers, fever, malaise and painful peripheral neuropathy. Painful neuropathy is associated with higher doses.^{37, 38}

Both these agents inhibit HIV replication without the frequent bone marrow suppression associated with AZT. These drugs may offer options to patients intolerant to AZT. They may also prove useful in the treatment of AZT-resistant strains of HIV. Both ddI and ddC are being rigorously studied in order to establish safety and efficacy and are available only for "compassionate use" outside of the clinical trials.³⁵

Fluconazole

The continuing search for effec-

tive, non-toxic anti-fungal agents has resulted in the development of the first orally available triazole, fluconazole. Fluconazole has many desirable features including its excellent bioavailability following oral absorption, high CSF levels, relative lack of toxicity, infrequent incidence of drug interactions, and prolonged serum half-life. The drug works like other imidazoles in that it interferes with a fungal cytochrome P-450 demethylase enzyme involved in the synthesis of a fungal membrane sterol known as ergosterol.³⁹ The drug has been shown to be efficacious against a variety of pathogenic mycoses, and has been approved by the FDA for the treatment of cryptococcal meningitis and candidal infections in immunocompromised patients.^{40, 41} While the relative merits of amphotericin B versus fluconazole in the treatment of cryptococcal meningitis remains debatable, fluconazole is clearly advantageous in the long term maintenance of cryptococcal meningitis in AIDS patients. The efficacy of fluconazole against a variety of other mycotic infections remains to be determined by large multicenter trials.³⁹⁻⁴¹

The drug has been well tolerated in clinical studies and is definitely less toxic than miconazole or ketoconazole. Occasional cutaneous reactions have occurred as have drug-induced hepatitis. Drug interactions include increased levels of phenytoin, cyclosporin and coumadin with the concomitant administration of fluconazole. This drug represents a major advance in the treatment of opportunistic mycoses.³⁹

Mefloquine

Malaria continues to be a major threat to human populations in developing countries. The rapid development of resistance to antimalarial drugs has thwarted

eradication projects and stimulated interest in the development of new antimalarial compounds and work on vaccine development. In 1990, the new antimalarial drug mefloquine was released for use in the United States. This drug is a quinolone-methanol derivative which is chemically related to quinine. It is particularly useful in the treatment and prevention of *Plasmodium falciparum*. This form of malaria is the most lethal and most likely to be resistant to other standard antimalarial agents. The drug has proven to be efficacious in the treatment of resistant strains of falciparum malaria as well as the prevention of infection when traveling in malaria endemic areas. The drug has an exceedingly long half life and may be given on a weekly or every other week basis in the prevention of malaria in travelers.⁴²

The drug is generally well tolerated but significant side effects have been reported. Minor gastrointestinal complaints and light-headedness and dizziness are frequently observed with this medication. Mefloquine has been associated with prolongation of the QT interval as well as sinus bradycardia. The drug should not be given in individuals using beta blocking agents, calcium channel blockers, or patients with altered cardiac conduction.⁴³

Other Recent Advances in the Treatment of Infectious Diseases

After two decades of debate and controversy, corticosteroids have now been convincingly demonstrated to be effective in preventing the complications of some forms of bacterial meningitis. Early treatment with dexamethazone in addition to antimicrobial agents decreases the frequency of neurosensory hearing loss in survivors with bacterial meningi-

Table 3. *Helicobacter pylori* and Gastrointestinal Disease

GI Pathology	Number of Patients Studied	Evidence of <i>H. Pylori</i> Infection (%)
No GI lesion	230	0-20
Active chronic gastritis	401	64-95
Gastric ulcer	78	35-86
Duodenal ulcer	46	75-100

Adapted from Reference #14.

tis. Efficacy of steroids in bacterial meningitis has only been shown for childhood meningitis with *Hemophilus influenzae* infection. The utility of this approach in the treatment of adults or in children with other forms of bacterial meningitis remains to be demonstrated.⁴⁴

Clinical trials with monoclonal antibodies against bacterial endotoxin or excess levels of tumor necrosis factor produced in gram negative sepsis have recently been undertaken. Multi-center, prospective trials investigating the value of a monoclonal antibody against the core glycolipid of LPS in the treatment of septic shock appear quite encouraging.⁴⁵ A pilot study using a monoclonal antibody against tumor necrosis factor-alpha in the treatment of septic shock has recently been published.⁴⁶ This novel immunotherapeutic approach to the treatment of septic shock offers an opportunity to improve the dismal survival statistics associated with endotoxic shock.

A new oral vaccine against typhoid fever has also been introduced into the United States in 1990. This is a live, attenuated, oral vaccine which is given to travelers or children in typhoid-endemic areas to prevent typhoid fever. The vaccine is made from a mutant strain of *Salmonella typhi* known as TY21A. This mutant bacterium is incapable of causing typhoid fever but induces an immune response to the orga-

nism which successfully protects recipients from infection with *S. typhi*.⁴⁷ A new generation of bacterial vaccines based upon recombinant DNA technology is anticipated within the next decade.

Conclusion

The 1990s offer an exciting opportunity to bring the advances in molecular biology and immunology into clinical practice. There is no greater challenge to medicine today than the epidemic of the Human Immunodeficiency Virus and its devastating consequences on the American population. The insights and discoveries of the 1980s offer a realistic hope of controlling the epidemic by the end of this century. Great strides have been made in the management of infectious diseases recently, and we anticipate that the promises of molecular biology will be realized in clinical medicine in the near future.

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References

- ¹ Centers for Disease Control. Update: Acquired immunodeficiency syndrome — United States, 1989. *MMWR* 1990; 39:81-86.
- ² Chu SY, Buehler JW, Berkelman RL. Impact of human immunodeficiency virus epidemic on mortality in women of reproductive age, United States. *JAMA* 1990; 264:225-229.
- ³ Volberding PA et al, and the AIDS clinical trials group of the National Institute of Allergy and Infectious Disease. Zidovudine in asymptomatic human immunodeficiency virus infection. *N Engl J Med* 1990;322:491-499.
- ⁴ Hirsch MS. The rocky road to effective treatment of human immunodeficiency virus infection. *Annals of Internal Medicine* 1989;110:1-3.
- ⁵ Larder BA, Darby G, Richman DD. HIV with reduced sensitivity to Zidovudine (AZT) isolated during prolonged therapy. *Science* 1989;243:1731-1734.
- ⁶ Bolognesi DP. Progress in vaccine development against SIV and HIV. *Journal of Acquired Immunodeficiency Syndromes* 1990;3:390-394.
- ⁷ Mayer KH, DeBuono BA. (editors) AIDS in Rhode Island. *Rhode Island Medical Journal* 1990;73:279-315.
- ⁸ McDade, JE. Ehrlichiosis — A disease of Animals and Humans. *J Infect Dis* 1990;161:609-617.
- ⁹ Centers for Disease Control: Human Ehrlichiosis: United States. *MMWR* 37:270-277, 1988.
- ¹⁰ Harkness JR, Ewing SA, Crutcher JM, Kudlac J, McKee G, Istre GR. Human ehrlichiosis in Oklahoma. *J Infect Dis* 1989;159:576-9.
- ¹¹ Centers for Disease Control. Rocky Mountain Spotted Fever and Human ehrlichiosis — U.S., 1989. *MMWR* 1990;39:281-284.
- ¹² Fishbein DB, Kemp A, Dawson JE, Greene NR, Redus MA, Fields DH. Human ehrlichiosis: Prospective active surveillance in hospitalized patients. *J Infect Dis* 1989;160:803-9.
- ¹³ Warren JR, Marshall BJ. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet* 1983;2:1273-1275.
- ¹⁴ Blaser MJ. *Helicobacter pylori* and the pathogenesis of gastroduodenal inflammation. *J Infect Dis* 1990;161:626-633.
- ¹⁵ Marshall BJ, Goodwin CS, Warren JR, Blincow ED, Phillips M, Murray R, Blackburn SJ, Waters TE, Sanderson CR. Prospective double-blind trial of duodenal ulcer relapse after eradication of *Campylobacter pylori*. *Lancet* 1988;2:1437-1445.
- ¹⁶ Coghlen JG, Gilligan D, Humphries H, McKenna D, Dooley C, Sweeney E, Keane C, O'Morain C. *Campylobacter pylori* and recurrence of duodenal ulcers — A twelve month followup study. *Lancet* 1987;2:1109-1111.
- ¹⁷ Grayston JT, Campbell LA, Kuo CC, Mordhorst CH, Saikku P, Thom DH, Wang SP. A new respiratory tract pathogen: *Chlamydia pneumoniae* strain TWAR. *J Infect Dis* 1990;161:618-625.
- ¹⁸ Grayston JT, Kuo CC, Wang SP, Altman T. A new *Chlamydia psittaci* strain, TWAR, isolated in acute respiratory tract infections. *N Engl J Med* 1986;315:1361-1368.
- ¹⁹ Grayston JT. *Chlamydia pneumoniae*, strain TWAR. *CHEST* 1989;95:664-669.
- ²⁰ Koutsky LA, Galloway DA, Holmes KK. Epidemiology of genital human papillomavirus infection. *Epidemiol Rev* 1988;10:122-163.
- ²¹ Jenison SA, Yu X, Valentine JM, Koutsky LA, Christiansen AE, Beckmann AM, Galloway DA. Evidence of prevalent genital-type human papillomavirus infections in adults and children. *J Infect Dis* 1990;162:60-69.
- ²² Douglas JM, Eron LJ, Judson FN, Rogers M, Adler MB, Taylor E, Tanner D, Deets E. A randomised trial of combination therapy with intralesional interferon-alpha and podophyllin versus podophyllin alone for the therapy of anogenital warts. *J Infect Dis* 1990;162:52-59.
- ²³ Anderson LJ. Human parvoviruses. *J Infect Dis* 1990; 161:603-608.
- ²⁴ Kurtzman GJ, Ozawa K, Cohen B, Hanson G, Oseas R, Young NS. Chronic bone marrow failure due to persistent B19 parvovirus infection. *N Engl J Med* 1987;317:287-294.
- ²⁵ Centers for Disease Control. Risks associated with human parvovirus B19 infection. *MMWR* 1989;38:81-89, 93-97.
- ²⁶ Alter HJ, Purcell RH, Shih JW, Melpolder JC, Houghton M, Choo QL, Kuo G. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. *N Engl J Med* 1989;321:1494-1500.
- ²⁷ Stevens CE, Taylor PE, Pindych J, Choo QL, Bradley DW, Kuo G, Houghton M. Epidemiology of hepatitis C virus: A preliminary study in volunteer blood donors. *JAMA* 1990;263:49-53.
- ²⁸ Davis GL, Balart LA, Schiff ER et al: Treatment of chronic hepatitis C with recombinant interferon alpha: A multicenter randomized, controlled trial. *N Engl J Med* 1989;1501-1506.
- ²⁹ Rayes GR, Purdy MA, Kim JP, Luk KC, Young LM, Fry KE, Bradley DW. Isolation of a cDNA from the virus responsible for enterically transmitted non-A, non-B hepatitis. *Science* 1990;247:1335-1339.
- ³⁰ Centers for Disease Control. Enterically transmitted non-A, non-B hepatitis — Mexico. *MMWR* 1987;36:597-601.
- ³¹ English CK, Wear DJ, Margileth AM, Lissner CR, Walsh GP. Cat-scratch disease: Isolation and culture of the bacterial agent. *JAMA* 1988;259:1347-1352.
- ³² Bogue CW, Wise JD, Gray GF, Edwards KM. Antibiotic therapy for cat-scratch disease? *JAMA* 1989;262:813-816.
- ³³ Koehler JE, LeBoit PE, Egbert BM, Burger TG. Cutaneous vascular lesions and disseminated cat-scratch disease in patients with acquired immunodeficiency syndrome in AIDS related complex. *Annals of Internal Medicine* 1988;109:449-455.
- ³⁴ Yamanishi K, Shiraki K, Condo T, et al. Identification of human herpes-virus-VI as a causal agent for exanthem subitum. *Lancet* 1988;1:1065-1067.
- ³⁵ Yarchoan R. et al. Clinical pharmacology of 3'-Azido- 2', 3' — dideoxythymidine (zidovudine) and related dideoxynucleosides. *N Engl J Med* 1989;321:726-738.
- ³⁶ Lambert JS et al. 2', 3' — Dideoxyinosine (ddI) in patients with acquired immunodeficiency syndrome or AIDS related complex. *N Engl J Med* 1990;322:1333-1339.
- ³⁷ Jeffries, DJ The antiviral activity of dideoxycytidine. *J Antimicrobiol Chemo.* 1989;23, SupplA 29-34.
- ³⁸ Dubinsky RM. Reversible axonal neuropathy from the treatment of AIDS and related disorders with 2', 3' — dideoxycytidine (ddC). *Muscle and Nerve* 1989;12:856-860.
- ³⁹ Galgiani JN. Fluconazole, a new antifungal agent. *Ann Intern Med* 1990;113:177-179.
- ⁴⁰ Sugar AM, Saunderson C. Oral fluconazole as suppressive therapy for disseminated cryptococcosis in patients with acquired immunodeficiency syndrome. *Am J Med* 1988;85:481-489.
- ⁴¹ Larsen RA, Leal AE, Chan LS. Fluconazole compared with amphotericin B plus flucytosine for cryptococcal meningitis in AIDS. *Annals of Internal Medicine* 1990;113:183-187.
- ⁴² Centers for Disease Control. Recommendations for the prevention of malaria among travelers. *MMWR* 1990;39(RR-3):1-10.
- ⁴³ Krogstad DJ, Herwaldt BL. Chemoprophylaxis in treatment of malaria. *N Engl J Med* 1988;319:1538-1540.
- ⁴⁴ Label MH, Freij BJ, Syrogiannopoulos GA, Chrane DF, Hoyt MJ, Stewart SM, Kennard BD, Olsen KD, McCracken GH. Dexamethasone therapy for bacterial meningitis. *N Engl J Med* 1988;319:964-971.
- ⁴⁵ Ziegler EJ. Protective antibody to endotoxin core: The Emperor's New Clothes? *J Infect Dis* 1988;158:286-290.
- ⁴⁶ Exley AR, Cohen J, Buurmann W, Owen R, Hanson G, Lumley J, Aulakh JM, Bodmer M, Riddell A, Stephens S, Perry M. Monoclonal antibody to TNF in severe septic shock. *Lancet* 1990;1:1275-1277.
- ⁴⁷ Cryz SJ, Furer E, Baron LS, Noon KF, Rubin FA, Kopecko DJ. Construction and characterization of a Vi-positive variant of the *Salmonella typhi* live oral vaccine strain TY21A. *Infect Immun* 1989;57:3863-3868.

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1. Data on file, G.D. Searle & Co.
2. 1988 Joint National Committee: The 1988 report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1988;148:1023-1038.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration.

Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°, 2°, 3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomastia, increased urination, spotty menstruation, impotence.

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Recent Advances in Gastroenterology

Edward R. Feller, MD

... interferon was effective in inducing a sustained loss of (hepatitis) viral replication with ... remission in over one-third of patients.

Bleeding Esophageal Varices

Bleeding esophageal varices commonly complicate portal hypertension and are associated with an in-hospital mortality of about 40% and a one-year survival of 30-40%. Esophageal varices result from the dilation of pre-existing embryonic venous channels in an attempt to decompress increased pressure in the portal venous system. Data support the use of pharmacologic therapy initially with vasopressin and nitroglycerin to lower portal pressure.¹ The addition of nitroglycerin to vasopressin potentiates the vasopressin-induced decrease in portal pressure and reverses its cardiotoxic effects. Somatostatin reduces splanchnic blood flow, and in some studies has been shown to decrease portal pressure and perhaps have comparable efficacy to vasopressin in the control of variceal bleeding.¹ While drug therapy may control early bleeding and allow time to stabilize a desperately ill patient, long-term survival requires more definitive treatment.

Edward R. Feller, MD, is Clinical Associate Professor of Medicine with Brown University Program in Medicine, Providence, Rhode Island.

A recent prospective study demonstrates a survival advantage in alcoholic patients undergoing endoscopic sclerosis of varices compared to surgery with a distal splenorenal shunt.² Patients failing sclerosis had surgical treatment. This study supports the use of sclerotherapy as an initial treatment modality in variceal hemorrhage with surgical approach available, if necessary. Failure of sclerotherapy is commonly due to bleeding from gastric varices or portal hypertensive gastropathy.

Another long-term pharmacologic approach to variceal bleeding is the use of beta-blockade to decrease portal pressure. In a recent study, 108 patients with varices that had stopped bleeding spontaneously before diagnostic endoscopy were randomized to oral propranolol (titrated to decrease resting pulse rate by 25%) or long-term injection sclerotherapy.³ In the propranolol group, 28 of 52 patients had recurrent bleeding with a total of 57 re-bleeding episodes. In the sclerotherapy group, 25 of 56 patients had repeat bleeding, with a total of 40 episodes. On an intention-to-treat basis, the risk of re-bleeding and survival were similar. Factors related to recurrent propranolol bleeding included the

height of the pretreatment resting pulse and the extent of reduction of pulse rate in response to propranolol. Current studies in progress combining sclerotherapy with long-term propranolol may yield data to support the use of dual therapy to decrease both early and late re-bleeding. Current evidence supports the concept that long-term survival after variceal hemorrhage requires definitive therapy. The role of sclerotherapy, chronic pharmacologic control, or surgery in individual patients is evolving.

Anti-Viral Therapy for Chronic Hepatitis

The chronic hepatitis B surface antigen carrier state affects about 5% of the world's population and as many as one million patients in this country. Only 20-40% of these individuals will have chronic liver disease and a smaller proportion will progress

ABBREVIATIONS USED:

BUN: blood urea nitrogen
DNA: deoxyribose nucleic acid
ESWL: extracorporeal shock wave lithotripsy
GI: gastrointestinal
HCV: hepatitis C virus
HIV: human immunodeficiency virus

to cirrhosis. The diagnosis of chronic hepatitis B rests on positive hepatitis B surface antigen in the serum, with hepatitis B virus DNA, or "e" antigen in the serum of patients with chronic (greater than six months) serum transaminase elevation; liver biopsy is useful in distinguishing this condition from the healthy hepatitis B carrier.

Multiple trials have shown that corticosteroids are not beneficial and likely detrimental to the course of chronic hepatitis B infection.⁴ However, recent studies support the possibility that interferon-alfa will be useful in this disease. The interferons are host proteins elaborated in response to antigenic stimuli, such as viral infection. Initial studies demonstrated that interferon led to clearance of viral particles from the blood with loss of hepatitis B surface antigen positivity associated with clinical improvement in the accompanying chronic liver disease and decrease in serum enzymes with histologic improvement.⁵ Controlled trials suggest that 25-50% of adult patients treated with a 3-to-6 month course of therapy have a serological response to treatment.⁶ However, relapse tends to occur when the therapy is withdrawn. A large recent randomized trial⁷ showed that interferon was effective in inducing a sustained loss of viral replication with clinical and histologic remission in over one-third of patients. In addition, about 10% of patients treated with interferon had disappearance of hepatitis B surface antigen from serum. Further studies are needed to decide which criteria should be utilized to determine whether a patient with chronic hepatitis B will benefit from this therapy.

Chronic infection by non-A, non-B hepatitis viruses has been postulated as a frequent cause of chronic liver disease. Recently an

assay for a non-A, non-B virus designated as the C virus (HCV) has been developed. To determine the prevalence and meaning of antibodies to HCV in patients with non-alcoholic chronic liver disease, the presence of anti-HCV antibodies was determined in a large recent study.⁸ In patients with unexplained chronic liver disease, the prevalence of anti-HCV antibodies was 82%, suggesting that HCV plays an important role in unexplained chronic liver disease. A major problem with non-A, non-B hepatitis is its propensity to progress to chronicity. Early studies using interferon^{9, 10} suggest that this treatment may result in an objective biochemical response rate in one-third of patients with concomitant improvement in liver histology. However, relapses occurred after therapy was stopped in the majority of individuals. Ongoing trials may help to determine the role of interferon in this disease. At present, anti-viral therapy of chronic viral hepatitis is a promising modality with treatment restricted to patients involved in clinical trials.

Modern Management of Ascites

Routine management of ascites in chronic liver disease has included diuretic therapy and sodium restriction. For refractory disease, some authors have advocated the peritoneal-venous shunt which transports ascites into the systemic circulation. However, the procedure has not gained wide acceptance because of frequent complications including coagulopathy, pulmonary edema, and septic complications with a procedure-related complication rate of greater than 50% in some studies.¹¹ A recent large trial comparing diuretics with shunts showed no statistical difference in long-term survival.¹²

Because of the problem of re-

fractory ascites and the difficulties of diuretic therapy, large volume paracentesis has been studied. Recent reports have demonstrated that 4 to 6 liter paracentesis results in no change in plasma volume, serum sodium or BUN concentration, or evidence of hypotension or encephalopathy.¹³ Large volume paracentesis was superior to diuretics for mobilizing ascites, decreasing morbidity and mortality, and was associated with a marked decrease in hospitalization in one large study.¹⁴ Because of concerns that removal of large amounts of fluid from the peritoneal cavity might result in deteriorating hemodynamics and renal function, a study was performed comparing periodic large volume paracentesis with and without intravenous albumin.¹⁵ Albumin seemed to protect against cardiac, renal, or encephalopathic problems. Current evidence supports the use of repeated large volume paracenteses of 3 to 5 liters, with intravenous albumin infusion as initial therapy for massive ascites, with diuretics used as maintenance therapy as needed.¹³

Should Alcoholics be Considered for Liver Transplantation?

Liver transplantation has assumed an increasing role in treatment of chronic liver diseases with an overall 5-year survival of approximately 70% reported in major centers. Candidates for transplantation include those with chronic viral liver disease, primary biliary cirrhosis, sclerosing cholangitis, and more controversially, selected patients with hepatic malignancy and alcoholic liver disease. A particularly controversial problem is that of the patient with chronic alcohol-induced liver disease. Alcohol abuse is the most common cause of liver failure in the United States. Transplantation centers have

been hesitant to accept alcoholic patients because of perceived problems of poor compliance, risk of recidivism, and the effects of alcohol injury on other organs. In a University of Pittsburgh study, 73 patients with alcohol-induced liver disease received orthotopic liver transplants.¹⁶ Seventy-one percent survived at 2-year follow-up, a figure similar to a non-alcohol transplant control group. Further studies may help define the role of transplantation in selected groups of patients, including those with alcohol-related liver problems.

Alcohol abuse is the most common cause of liver failure in the United States.

Alternative Management of Gallstones

Both postmortem and ultrasound examinations in diverse populations in this country and in Western Europe have demonstrated that as many as 20% of women and 10% of men above the age of 50 have gallstones. Frequently, however, gallstones are asymptomatic and no treatment is warranted.¹⁷ The traditional management of choice for symptomatic cholelithiasis has been cholecystectomy, performed an estimated 500,000 times per year in the United States. Recently, multiple alternative treatments, including extracorporeal shock-wave lithotripsy (ESWL), oral cholesterol solubilizing agents and contact dissolving agents, as well as laparoscopic cholecystectomy, have been introduced as possible management modalities¹⁸ (Table 1).

Alternatives to surgical cholecystectomy are only effective for cholesterol stones. Stone-dissolving agents increase the bile salt pool and decrease hepatic secretion of cholesterol in bile. Hos-

pitalization is not required, but dissolution is slow, requiring a minimum of 6 months and is associated with a dissolution success rate of 10 to 50% in reported series.¹⁹ The second generation drug, ursodeoxycholic acid, at a recommended dosage of 600 mg per day is associated with a cholesterol gallstones dissolution rate of about 1 mm per month. Such oral bile acid dissolution therapy is not effective when gallstones are calcified or when the cystic duct is obstructed. This therapy is well tolerated and can be continued chronically because of the absence of major side effects. In the elderly, high risk patient, oral dissolution therapy is a practical treatment alternative to surgical management for symptom relief. Cost, duration of therapy, the possibility of recurrence, and uncertain side effects may limit wide use.

Disintegration of gallstones by ESWL is undergoing clinical trials in more than 30 North American centers. A recent review assesses 21 studies in human subjects.²⁰ ESWL safely fragments stones in 80 to 100% of selected patients. However, the rate of satisfactory fragmentation varies widely from 22 to 78% in different series depending on the characteristics of the stone population. For solitary stones less than 20 mm in diameter, 90% of individuals will be stone-free within 6 to 9 months. At present, the technique is limited to patients with less than 3 non-calcified gallstones, each having a maximum diameter of 25 to 30 mm. About 10 to 20% of gallstone patients meet these current criteria. Shock-wave lithotripsy has the advantage of being an out-patient procedure without general anesthesia. Lithotripsy of common bile duct stones is currently reserved for cases in which endoscopic sphincterotomy has failed. Lithotripsy must be fol-

lowed by oral bile acid dissolution therapy to prevent recurrence since the underlying cause of gallstone formation has not been eliminated.

Removal of an intact gallbladder via a laparoscopic procedure is a new and promising technique.

Methyl-tert-butyl ether is a powerful cholesterol solubilizing agent which can be infused directly into the gallbladder via a percutaneously placed catheter under ultrasound guidance. Advantages are that dissolution may be possible within hours, and the number of stones in the gallbladder is not a limiting factor. However, this treatment is invasive with possible procedure-related complications, including bleeding, bile leak, infection, and intravascular hemolysis secondary to the solvent. It is likely to find maximum usefulness in acutely ill, debilitated patients.

Removal of an intact gallbladder via a laparoscopic procedure is a new and promising technique. The required incision is small, and hospitalization is brief. This modality is new, still considered experimental, but may eventually be a treatment of choice in uncomplicated gallbladder disease in patients without prior abdominal surgery.

Cholecystectomy remains the treatment of choice because it is effective regardless of type and number of stones while eliminating the possibility of recurrence. Mortality ranges have been in the range of 0.2 to 0.4% with a recurrence rate of approximately 5%. Individual patient selection is vital in determining which gallstones require treatment and which modality is most appropriate for the individual patients. Ongoing clinical trials may provide clearer data and help to se-

lect specific options for individual patients in the future.

Is Duodenal Ulcer An Infectious Disease?

The presence of *Helicobacter pylori* in the upper gastrointestinal tract is commonly encountered in patients with gastritis and duodenal ulcer disease. Data suggests that this organism may be an etiologic agent in many cases of gastritis and duodenal ulcer. A study of prevalence of *H. pylori* in asymptomatic patients revealed a higher rate in those with histologic abnormalities, suggesting an etiologic role.²¹ In duodenal ulcer, a review of 10 published studies showed a mean *H. pylori* carriage rate of 86%.²² However, patients with duodenal ulcer also have higher mean stimulated acid output, parietal cell mass, and nocturnal acid secretion than normal individuals. Abnormal acid secretion may induce gastric metaplasia within the duodenal cap, allowing the bacterium to colonize the duodenum from its more usual habitat in the antrum of the stomach; thus, duodenal inflammation is initiated. Studies have shown virtually all patients

with duodenal ulcer have evidence of gastric inflammation and *H. pylori* infestation. Eradication seems to reduce the recurrence rate of duodenal ulcer. In one study, 50 patients with intractable duodenal ulcer were randomly assigned to 4 weeks of treatment with colloidal bismuth subcitrate alone or with amoxicillin and metronidazole to eradicate this infection.²³ *H. pylori* was eradicated in 17 of 45 without a relapse in 12 months. The relapse rate for duodenal ulcer was higher (89%) among patients remaining positive for *H. pylori*. Though acid suppression for four to eight weeks heals most duodenal ulcers, the relapse rate is high. Concomitant eradication of *H. pylori* may reduce recurrence rate.

Current evidence suggests that the clinician should suspect *H. pylori* in all patients with dyspepsia. Current data indicates that this organism is a common cause of chronic gastritis and that its eradication may reduce the relapse rate in duodenal ulcer. Nonulcer dyspepsia is a pleomorphic clinical problem. Some patients will have underlying infection, though the prevalence of this is unclear.

The diagnosis is made by biopsy which should be multiple since the lesions are patchy in distribution. At present, results suggest that therapy for clinical gastritis and duodenal ulcer should revolve around healing the ulcer with conventional medication. It remains unclear which patients with duodenal ulcer and documented *H. pylori* should be treated, which tests should be utilized to follow them after eradication, and what constitutes optimal management of patients who do not respond or who develop a recurrence. In refractory patients, specific therapy directed toward eradication of infection may bring clinical relief and histologic resolution. Initial treatment currently recommended is 2 tablets of bismuth subsalicylate, 4 times daily chewed on an empty stomach for 10 to 14 days plus metronidazole, one gram per day in divided doses. The combination eradicates infection in approximately 70% of patients. Addition of tetracycline, 500 mg, 4 times daily may increase the response rate to 80 to 90%. A single agent is less likely to be effective.

Table — Therapy for Symptomatic Cholelithiasis

Treatment Modality	Mechanism of Action	Composition of Gallstones Amenable to Treatment	Invasive Therapy	Hospitalization Required	Factors Responsible for Gallstone Formation Eliminated After Treatment
Cholecystectomy	Removal of Gallstones	All: cholesterol, pigment, mixed	Yes	Yes	Yes
Oral cholelitholytic agents (chenodiol, ursodiol)	Increase of bile salt pool Decrease of hepatic secretion in bile	Cholesterol only (especially floating, small type)	No	No	No
Extracorporeal shock wave lithotripsy	Stone fragmentation Fragment passage from gallbladder?	Cholesterol (especially single stones); Probably mixed	No	Probably no (after investigational phase)	No
Methyl-tert-butyl ether	Direct contact dissolution	Cholesterol	Yes	Variable (brief)	No

Evaluation of Gastrointestinal Bleeding

Guidelines for hemoccult screening for occult blood in the stool are evolving. The major imperative in performing yearly tests for occult blood in asymptomatic patients above the age of 45 is to detect colorectal neoplasia. A large recent population study found that an asymptomatic patient 45 years of age or older with a positive Hemoccult test has about a 10% chance of having colorectal carcinoma and a 33% chance of having either carcinoma or a benign polyp.²⁴ However, if Hemoccult slides are the only screening test used, 50 to 60% of lesions will go undetected, since not all cancers bleed or bleed continually. Although multiple controlled trials of stool occult blood screening have documented a higher percentage of early, favorably staged carcinoma among screened patients, no concomitant decrease in mortality from colon cancer in screened populations has been shown.²⁴ Ulceration of carcinoma may be required before occult blood testing may be positive, and irregular distribution of blood in specimens may be present thus leading to a possible sampling error.

Among patients 55 years or older, initial colonoscopy had a great diagnostic yield and was more effective for the detection of colon polyps or cancer compared to flexible sigmoidoscopy combined with air contrast barium enema.

In patients with suspected non-emergent lower GI bleeding, the entire colon must be visualized to evaluate the possibility of neoplasm. A randomly controlled trial was performed comparing diag-

nostic yield and cost effectiveness of strategies for evaluation of non-emergent lower GI bleeding.²⁵ Among patients aged 55 years or older, initial colonoscopy had a greater diagnostic yield and was more effective for the detection of colon polyps or cancer compared to flexible sigmoidoscopy combined with air contrast barium enema. However, for younger patients, cancer was less common (1% vs 8% in the older age group); thus, flexible sigmoidoscopy and air contrast barium enema may be more cost effective for younger patients.

Approach To Diarrhea In HIV Infection

Diarrhea is the most common gastrointestinal symptom in patients with the acquired immune deficiency syndrome (AIDS), occurring in up to 50% of patients followed longitudinally. Diarrhea may occur in association with rectal tenesmus in the context of proctitis or with abdominal cramps and bleeding in colitis. A wide range of causes, including opportunistic infections, has been documented.

A recent study compares the efficacy and cost effectiveness of alternative management schemes using a decision analysis model.²⁶ Comparison was made between (1) a full evaluation, including stool culture, stool determination for OVA and parasites, a protozoa stain, upper GI endoscopy with biopsy, colonoscopy with biopsy; (2) limited evaluation which includes stool culture, stool determination for OVA and parasites, and a stool stain for protozoa; and (3) a minimal evaluation, including stool culture. Patients without a diagnosis were treated with a semi-synthetic narcotic, antidiarrheal agent. Remission rates were approximately 75% in each evaluation group. Respective

costs for the full limited and minimal evaluations were \$5,419, \$1,997, and \$1,700 per patient. These data suggest that one should reserve full evaluation for non-responders to symptomatic treatment.

References

- ¹ Burroughs, AK: The management of bleeding due to portal hypertension, Part I, The management of acute bleeding episodes. *Quart J Med* 1988;254:447-458.
- ² Henderson, JM: Endoscopic variceal sclerosis compared with distal splenorenal shunt to prevent recurrent variceal bleeding in cirrhosis. *Ann Intern Med* 1990; 112:262-269.
- ³ Westaby, D, Polson, RJ, Gimson, AES, et al: A controlled trial of oral propranolol compared with injection sclerotherapy for the long-term management of variceal bleeding. *Hepatology* 1990;11:353-359.
- ⁴ Lam, KC, Lai, CL, Ng, RP, et al: Deleterious affect of prednisolone in hepatitis B surface antigen positive chronic active hepatitis. *N Engl J Med* 1981;304:380-386.
- ⁵ Alexander, GJM, Fagan, EA, Daniels, HM, et al: Loss of hepatitis B surface antigen with interferon therapy in chronic hepatitis B virus infection. *Lancet* 1987;2:66-68.
- ⁶ Hoofnagle, JH, Peters, M, Mullen, KD, et al: Randomized control trial of recombinant human alpha interferon in patients with chronic hepatitis B. *Gastroenterology* 1988;95:1318-25.
- ⁷ Perrillo, RP, Schiff, ER, Davis, GL, et al: A randomized control trial of interferon alpha-2b alone and after prednisone withdrawal for the treatment of chronic hepatitis B. *N Engl J Med* 1990;323:295-301.
- ⁸ Sanchez-Tapias, JM, Barrera, JM, Costa, J, et al: Hepatitis C virus infection in patients with non-alcoholic chronic liver disease. *Ann Intern Med* 1990;112:921-924.
- ⁹ Davis, GL, Balant, LA, Schiff, ER, et al: Treatment of chronic hepatitis C with recombinant interferon alpha. A multicenter randomized controlled trial. *N Engl J Med* 1989;321:1501-1506.
- ¹⁰ DiBisceglie, EAM, Hoofnagle, JH: Anti-viral therapy of chronic viral hepatitis. *Amer J Gastro* 1990;85:650-654.
- ¹¹ Scholz, DG, Nagorney, DM, Linder, KD: Poor outcome from peritoneovenous shunting for ascites. *Amer J Surg* 1980; 139:125-131.
- ¹² Stanley, MM, Ochi, S, Lee, KK, et al: Peritoneovenous shunting as compared with medical treatment in patients with alcoholic cirrhosis and massive ascites. *N Engl J Med* 1989;321:1632-1638.
- ¹³ Kellerman, PS, Linas, SL: Large volume paracentesis in treatment of ascites. *Ann Intern Med* 1990;112:889-891.
- ¹⁴ Gines, P, Arroyo, V, Quintero, E, et al: Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites. Results of a randomized study. *Gastroenterology* 1987;93:234-41.

- ¹⁵ Gines, P, Tito, L, Arroyo, V, et al: Randomized comparative study of paracentesis with and without intravenous albumin in cirrhosis. *Gastroenterology* 1989;97:158-162.
- ¹⁶ Kumar, S, Stauber, RE, Gavalier, JS, et al: Orthotopic liver transplantation for alcoholic liver disease. *Hepatology* 1990;11:159-164.
- ¹⁷ Ransohoff, DF, Gracie, WA, Wolfenson, LB, et al: Prophylactic cholecystectomy or expectant management for silent gallstones. *Ann Intern Med* 1983;99:199-207.
- ¹⁸ Zuccaro, G: Alternative therapies for cholelithiasis. *Consultant* 1990;34:69-76.
- ¹⁹ Tint, GS, Salen, G, Colalillo, A, et al: Ursodeoxycholic acid: A safe and effective agent for dissolving cholesterol gallstones. *Ann Intern Med* 1982;97:351-356.
- ²⁰ Barkun, ANG, Ponchon, T: Extracorporeal biliary lithotripsy: A review of experimental studies and a clinical update. *Ann Intern Med* 1990;112:126-137.
- ²¹ Dooley, CP, Cohen, H, Fitzgibbons, PL: Prevalence of *helicobacter pylori* infection and histologic gastritis in asymptomatic persons. *N Engl J Med* 1989;321:1562-1566.
- ²² McKinlay, AW, Upadhyay, R, Gemmell, CG, et al: *Helicobacter pylori*: Bridging the credibility gap. *Gut* 1990;31:940-945.
- ²³ Rauws, EAJ, Tytgat, GNJ: Cure of duodenal ulcer associated with eradication of *helicobacter pylori*. *Lancet* 1990;335:1233-1235.
- ²⁴ Allison, JE, Feldman, R, Tekawa, IR: Hemoccult screening in detecting colorectal neoplasms: Sensitivity, specificity, and predictive value. *Ann Intern Med* 1990;112:328-333.
- ²⁵ Rex, DK, Weddle, RA, Lehman, GA et al: Flexible sigmoidoscopy plus air contrast barium enema versus colonoscopy for suspected lower gastrointestinal bleeding. *Gastroenterology* 1990;98:855-860.
- ²⁶ Johanson, JF, Sonnenberg, A: Efficient management of diarrhea in the acquired immunodeficiency syndrome. A medical decision analysis. *Ann Intern Med* 1990;112:942-948.

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Recent Advances in Pulmonary Medicine

Michael A. Passero, MD

The discovery of the gene (for cystic fibrosis) should make it possible to understand the control of ion-transport pathways to this disease.

At the recent national pulmonary disease meetings, over 4,000 abstracts were presented. This explosion in knowledge cannot be mastered by the specialist in the field. This review is therefore offered as an attempt to relate some important recent developments that may be of use in clinical practice.

Basic Science

The major breakthrough in pulmonary medicine in the last 12 months has been the identification of the cystic fibrosis gene. Cystic fibrosis (CF) is an autosomal recessive genetic disorder that occurs in one out of 2,000 live births. One of the puzzles of this illness has been the abnormal sweat electrolytes and the abnormally high electrical potential differences across epithelial surfaces of the respiratory tract and the sweat glands. Teams of investigators, working together,

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published the sequence of a portion of DNA from chromosome 7 that codes for a polypeptide of 1,480 amino acids and a molecular mass of 168,138 daltons.¹⁻³ This protein is similar to the mammalian multi-drug resistance P-glycoproteins and a number of other membrane associated proteins, suggesting that the CF protein is likely to be involved in the transport of ions across epithelial membranes. The protein has been named the cystic fibrosis trans-membrane conductance regulator. So far, the data suggest that this protein may either be an ion channel itself, or may serve to regulate ion channel activities. Compared to the protein in normals, the protein in most CF patients contains a deletion of a phenylalanine. The discovery of the gene should make it possible to understand the control of ion-transport pathways in this disease. In addition, a better test for carriers of the gene probably will be developed.

Tuberculosis

Approximately 22,000 new cases of tuberculosis are reported nationally each year. New developments in drug therapy have made shorter treatment courses now more reliable. A regimen con-

sisting of Rifampin, Isoniazid, and Pyrazinamide, in the initial phase of at least two months, followed by Isoniazid and Rifampin for a total of 6 months of therapy, is highly effective in treating tuberculosis.^{4,5} In addition, therapy can be given intermittently beginning as early as the third week. In patients with both tuberculosis and HIV infection, the early evidence

ABBREVIATIONS USED:

AIDS: acquired immune deficiency disease
ARDS: adult respiratory distress syndrome
CF: cystic fibrosis
COPD: chronic obstructive pulmonary disease
DNA: deoxyribonucleic acid
FDA: Food & Drug Administration
FEV-1: forced expiratory volume in 1 second
FVC: forced vital capacity
HIV: human immunodeficiency virus
IMV: intermittent mandatory ventilation
IPPB: intermittent positive pressure breathing
MICU: medical intensive care unit
PEEP: positive end expiratory pressure

indicates that short course regimens might be effective. However, at the present time, these patients should be treated for longer than 6 months because they are severely immuno-suppressed.

Approximately 22,000 new cases of tuberculosis are reported nationally each year.

The role of surgery in resistant tuberculosis has been reevaluated. Iseman et al reviewed the course of 99 patients with pulmonary disease caused by multiple drug-resistant strains of *Mycobacterium tuberculosis*.⁶ Twenty-nine of these patients had resection to supplement chemotherapy. Although the patients were treated preoperatively with multiple drug regimens in an effort to reduce the burden of organisms, 20 of 29 were still sputum culture positive at the time of surgery. Of the 27 survivors, 25 remained sputum culture negative for a mean duration of 36 months. Iseman et al concluded that resectional surgery appears to offer benefit to patients with pulmonary disease caused by *M. tuberculosis* with high levels of drug resistance.

Unfortunately, the use of a new anti-tuberculosis drug rifabutin, also known as ansamycin, has been disappointing in patients with *Mycobacterium avium* complex pulmonary disease.⁷ Rifabutin has good *in-vitro* activity against most clinical *Mycobacterium avium* complex isolates. In 406 patients with severe progressive *Mycobacterium avium* complex pulmonary disease that had been unresponsive to standard therapy, treatment with rifabutin resulted in greater sputum conversion and clinical improvement. In most cases, the drug did not have a marked effect on outcome. Additional controlled clin-

ical trials will be necessary to determine the proper use of rifabutin in this disease.

AIDS

The literature on AIDS is beyond the scope of this review, but the following studies are of special interest.

Recent attempts to improve the delivery of aerosolized pentamidine have led to some success with reduction in the usual adverse side effects.⁸ In many patients, the cough, breathlessness, and effect on pulmonary function after aerosolization of 150 mg of pentamidine lead to poor compliance with treatment. Simonds et al discovered that altering droplet size by the use of a baffle valve would greatly improve the optimal droplet size range. This approach offers the advantage of enhancing alveolar targeting while reducing large airways deposition and related side effects.

Stover et al⁹ proposed a simple exercise test for the screening for pneumocystis carinii pneumonia in patients with AIDS. They recommended a resting and an exercise blood gas after the patient exercised for 1.5 minutes using the Masters two-step staircase. An abnormal test was an increase in the exercise (A-a)O₂ gradient, or a less than 5 mm Hg decrease in the gradient from rest to exercise. A normal test eliminated *pneumocystis carinii* pneumonia from the differential diagnosis, but an abnormal test separated out a group of patients who needed additional diagnostic procedures because pneumocystis was a likely possibility.

Asthma

Many patients with asthma experience their worst attacks at night and in the early morning. Nighttime delivery of medications is an important concept. A recent study by D'Alonzo et al¹⁰ com-

pared the use of twice daily dosing of a conventional sustained-release theophylline compared with a chrono-therapeutically optimized sustained-release formulation administered at 8 pm in the evening. In this randomized study, the conventional twice daily dosing produced a relatively constant serum theophylline level over the 24 hours. In contrast, the 8 pm dosing was associated with larger peak-to-trough level fluctuation, with the higher levels occurring several hours after the drug was given, and the lower ones occurring at the end of the dosing interval. Between 2 and 6 am, peak expiratory flow and FEV-1 were significantly greater with the 8 pm dosing than with the twice daily dosing. This correlated with the serum theophylline level. The authors concluded that the chrono-therapeutically prescribed drug given at 8 pm in the evening resulted in better airflow levels overnight than the twice daily dosing. Importantly, there was no deterioration of airflow in the afternoon.

One should be aware that the young seem to be at risk for death from asthma in the summer months.

Asthma mortality remains an important problem. Weiss et al¹¹ reviewed reports of hospitalizations for asthma and deaths for asthma from the US Vital Statistics occurring from 1982 through 1986, and averaged the morbidity and mortality by month. Seasonal trends of morbidity and mortality were similar by sex, race, and geographical region, but differed significantly by age. In adults, age 65 years and older, most hospitalizations and deaths occurred between January and April. In younger persons (age 5 to 34 years), hospitalizations peaked

from September through November, but the deaths peaked between June and August. Weiss felt that the abnormal summer pattern may be related to atopic factors and the loss of family, school and medical supervision during the summer. One should be aware that the young seem to be at risk for death from asthma in the summer months.

Over the past several years, physicians have recognized that women with asthma show premenstrual deterioration of their asthma symptoms and lung function. Pauli et al studied lung function for several menstrual cycles in asthmatic women and healthy controls.¹² They found that the asthma group showed a significant deterioration with wheezing, coughing, shortness of breath, and chest tightness, and their morning peak expiratory flow rates were reduced. They showed no change in reactivity to methacholine during these times. The control group showed no changes in any parameters. The asthmatic women were not aware of having any symptoms of premenstrual asthma. Physicians should be aware of this phenomena in treating female patients with asthma.

Chronic Obstructive Pulmonary Disease

Mucous secretion is an important problem for patients with COPD. For many years pulmonologists were reluctant to prescribe expectorants and mucolytics because of lack of proven efficacy. New interest has arisen in these drugs, however. Recent studies suggest that iodinated glycerol may be useful in enhancing sputum expectoration by reducing mucus viscosity.¹³ This may be particularly useful in a patient with a very low FEV-1 who has trouble raising sputum. Side effects include increased serum iodide levels, acne, stomach upset, and

thyroid gland enlargement, but these are rare.

Gong¹⁴ has summarized problems of patients with chronic pulmonary disease who are clinically stable at sea level, but may become acutely ill while flying at decreased barometric pressure. Commercial planes, while cruising at 30-40,000 feet altitude, have cabin pressures that simulate altitudes of 5,000 to 10,000 feet. Gong points out that, in a healthy person with an SAO_2 of 97%, a fall of 9% is expected at 8,000 feet, and 12% at 10,000 feet. The oxygen saturation would still be adequate at 85%. However, in a patient who has COPD who normally has an oxygen saturation of 92%, the saturation will decrease by 12% and 25% at 8,000 and 10,000 feet respectively, to 67%. This can fall even further if the patient who has COPD walks in the cabin or falls asleep during the flight. Gong lists a number of respiratory contraindications to air travel. These include conditions that are adversely affected by hypoxemia such as active bronchospasm; conditions adversely affected by pressure changes, such as recent thoracic surgery; and inadequate pulmonary function as evidenced by a diffusion capacity of less than 50%; hypercapnia with a PCO_2 greater than 50; hypoxemia while breathing room air with a PO_2 less than 50; a maximum voluntary ventilation of less than 40 liters per minute, and a vital capacity less than 50% predicted. Gong recommends measuring the PO_2 as close to the time of flight as possible to predict what the PO_2 might be at altitudes of up to 10,000 feet. He developed a multiple regression equation for this prediction. He also recommends using hypoxic gas mixtures of oxygen and nitrogen to simulate the inspired oxygen tension at the anticipated altitude as part of the pre-flight testing.

Intensive Care

Recognition and treatment of multi-system disease has become a major theme in Intensive Care Units. Tran et al evaluated the effects of age, chronic disease, sepsis, organ system failure, and mortality in a medical-intensive care unit.¹⁵ In a retrospective study of 487 MICU patients, advancing age and pre-existing chronic disease were risk factors for multi-organ system failure. Sepsis was an independent predictor of multi-organ system failure, although 35% of patients with multi-organ system failure did not have sepsis. Eighty-three percent of the non-surviving patients had multi-organ system failure. The authors suggest that age, prior chronic disease, and extent of organ system failure rather than admission variables may be independent factors in mortality prediction in the intensive care unit.

Dark and Pingleton¹⁶ reviewed the incidence of non-hemorrhagic enteric complications in 124 patients with respiratory failure. Fifty-one percent of the patients had diarrhea, 50% had decreased bowel sounds, and 46% had abdominal distension. Pneumonia had caused the respiratory failure in 28% of patients and these patients had an average of five complications per patient. Whether antibiotics caused the diarrhea was not clear. Of the 81 patients whose serum albumin had been measured, only nine had normal levels. Hypoalbuminemia may be associated with diarrhea because the fall in serum albumin results in gastrointestinal mucosa edema. This causes changes in the mucosal membrane and fluid is exuded into the intestinal lumen. The recommendation is to use a peptide-based feeding formula that can reduce intestinal protein loss and is also better tolerated.¹⁷

Pressure support ventilation is

a relatively new form of mechanical ventilation where a selected amount of inspiratory pressure from 0 to 100 centimeters of water is provided during the inspiratory phase. When the patient initiates the breath, the selected amount of positive pressure is provided during inspiration at a very high on-demand flow rate until a certain minimum inspiratory flow rate is reached. The breath is then terminated. The patient controls inspiratory flow rate, inspiratory time, tidal volume and respiratory rate, so pressure support ventilation is really a modified boost of spontaneous ventilation. The difference between pressure-support ventilation and intermittent positive pressure breathing (IPPB) is that with pressure-support ventilation the amount of pressure delivered is maintained throughout inspiration and the inspiratory flow rate determines the time of inhalation, whereas with IPPB the breath is terminated when the preset pressure is reached. Pressure-support ventilation has been thought to result in better endurance conditioning of the respiratory muscles. However, no objective data exists to support this hypothesis. Probably the single major advantage of pressure support ventilation is that it allows a reduced work of breathing when the patient is breathing through an endotracheal tube. Thus, it may be helpful in weaning some patients and may be an alternative to IMV or T-piece trials. Pressure support ventilation results in positive pressure in the thorax, so venous return to the right heart may be impaired. Further studies will be needed to properly evaluate the role of pressure-support ventilation in critically ill patients.¹⁸

Another area that has become prominent in modern ventilator management has been the attempt to eliminate Auto-PEEP.

Auto-PEEP refers to the positive end-expiratory pressure created when the expiratory time is reduced to the point where complete exhalation doesn't occur before the next inspiratory cycle is initiated. The resultant positive pressure throughout the respiratory cycle during mechanical ventilation may actually be detrimental to the patient. The clinician must be aware of this phenomenon. Attempts to devise a simple way to measure Auto-PEEP have not yet been successful.¹⁹

Hoffman et al²⁰ attempted to evaluate the risk of Cheyne-Stokes respiration in patients with pulmonary edema. They studied 95 patients who had acute cardiogenic pulmonary edema requiring mechanical ventilation. After recovery, Cheyne-Stokes respiration was detected in 42 patients. There was no difference in the need for reinstitution of mechanical ventilation or inhospital mortality when patients with Cheyne-Stokes respiration were compared to those with normal respiration. In addition, in 58 patients for whom echocardiograms were available, there was no difference in the estimate of left ventricular ejection fraction between those patients with Cheyne-Stokes respiration and those patients without.

Hanley et al²¹ studied Cheyne-Stokes respiration in patients with congestive heart failure and concluded that nocturnal oxygen therapy can correct any hypoxemia that occurs and reduces the duration of the Cheyne-Stokes respiration.

Most physicians believe that Adult Respiratory Distress Syndrome results in few adverse long-term pulmonary consequences for survivors. Peters et al²² studied pulmonary function tests in 39 survivors of the adult respiratory syndrome in whom data had been prospectively collected during the

acute episode. The pulmonary function study stabilized within 6 months of the episode, and returned to normal in most survivors. Persistent abnormalities were found after 6 months in diffusing capacity in 61% of patients; in vital capacity, 43%; and in total lung capacity, 21%. These long-term abnormalities of pulmonary function of survivors of ARDS were not related to the initial lung impairment, but were directly related to persistence of impaired lung function during the acute episode. Recovery of lung function may also have been affected by the occurrence of sepsis.

Cancer

Burkey et al have reviewed the role of nocardial infection in patients with neoplastic disease.²³ They point out that nocardia is known to occur in patients receiving cytotoxic therapy, but it may also occur in patients with solid tumors in the absence of steroids or cytotoxic agents. Accordingly, nocardia should be suspected in patients who have pulmonary infiltrates or who have abscess formation, particularly those that develop after broad spectrum antibiotic therapy, or in patients with skin or brain infection associated with pulmonary infiltrates. Of 14 patients reviewed who had tumors plus nocardial infection, 11 had the infection diagnosed anti-mortem and were successfully treated with sulfonamides or trimethoprim-sulfamethoxazole.

Rickles reviewed the evidence supporting the association of cancer and clinical thrombophlebitis or "hypercoagulable" states.²⁴ He points out that there is now evidence for thrombogenic properties of plasma isolated from cancer patients. In one study, 13 out of 42 patients with various histologic types of lung

cancer had elevated plasma levels of fibrinogen and fibrin-degradation products, as well as elevated platelet counts. Their plasma produced major pulmonary thromboses and death when injected intravenously into mice or Guinea pigs. The investigators have partially characterized a factor called thrombosis-inducing activity, although further work needs to be done in this area. These data suggest that cancer may generate active products of clotting and that, at least in some patients, anticoagulation may be a necessary treatment feature.

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Minna reviewed the genetic events in the pathogenesis of lung cancer.²⁵ These include chromosomal and DNA deletions involving the recessive or tumor-suppressor genes, oncogene activation, and autocrine growth factors, such as gastrin-releasing peptide, and the associated inheritance of the high metabolic phenotype of 4-debrisoquine hydroxylase. Minna concludes that lung cancer cells have accumulated a series of genetic events that activate the dominantly-acting cellular proto-oncogenes on the one hand, while another group of changes seems to inactivate a second class of genes that appear to be recessive and referred to as the deletion, or tumor-suppressive genes. Alterations in both appear necessary for malignant transformation. In addition, autocrine growth factors and transcription factors regulated by tumor promoters are also produced by lung cancer cells.

Pharmacology

New drugs are one of the exciting aspects of pulmonary medicine. One recent discovery is that antihistamines, particularly those that are non-sedating, such as azelastine, cetirizine, ketotifen, terfenadine, and astemizole, as well as the classic antihistamines chlorpheniramine and hydroxyzine, can all protect against bronchial challenge induced by histamine.²⁶ Azelastine seems to be particularly promising in that it can also block exercise-induced bronchospasm and produce an increase in FEV-1. Azelastine is currently used in Japan and is awaiting FDA approval. Tinkelman et al²⁷ evaluated the safety and efficacy of multiple doses of azelastine in adult patients with bronchial asthma over time. All azelastine groups had significant reduction of other asthma medicines after one week. In the 4 mg and 6 mg BID groups, this reduction was sustained for 12 weeks. As our experience with these drugs increases, we may be able to include them in anti-asthma regimens.

Another new drug for asthma is nedocromil sodium, also awaiting FDA approval. In addition to interfering with the classical model of intermediate hypersensitivity, nedocromil sodium seems to inhibit antigen-induced bronchoconstriction and the activation of atypical mast cells and neutrophils, reminiscent of the nonsteroidal anti-inflammatory agents. A recent study²⁸ reported a consecutive sample of 127 patients with long-term asthma who were treated with nedocromil sodium. These patients were maintained on sustained release theophylline preparations and inhaled oral beta-adrenergic bronchodilators. The patients receiving nedocromil had a reduction in day and night time asthma, cough, concomitant bronchodilator

usage, and had improved objective measurements of lung function.

A promising new drug is formoterol, a new long-acting beta 2 agonist.²⁹ This drug seems to be particularly useful in smokers. The drug induces a bronchodilator effect lasting for more than 10 hours, significantly longer than albuterol. In addition, formoterol had a rapid onset of action.

The use of high doses of inhaled corticosteroids in asthma has become more widespread. For some patients, the usual doses of inhaled corticosteroids, such as beclomethasone dipropionate at 400 micro grams a day, are not always effective. Several authors have proposed using higher doses in these patients. Salmeron et al³⁰ published a multicenter randomized double blind study of inhaled beclomethasone dipropionate at the 1,500 microgram per day level, compared to placebo in 43 chronic asthmatic patients uncontrolled by inhaled salbutamol and oral theophylline. The patients were first given prednisone, and the study was designed to see whether the inhaled steroids could maintain the clinical improvement and optimal pulmonary function induced by prednisone. In patients who received the inhaled corticosteroids at high doses, the FEV-1 and peak expiratory flow remained above the optimal post-prednisone value with a trend toward improvement. In patients who received the placebo, the pulmonary functions decreased and remained below the optimal value. The authors concluded that in chronic asthma, inhaled beclomethasone dipropionate at the 1,500 microgram per day level may be useful in patients who do not respond to lower doses.

An important advance in respiratory pharmacology has been the use of long-term methotrexate

treatment in corticosteroid-dependent asthma. In a recent study by Mullarkey et al³¹ Cushingoid asthmatics who needed daily prednisone and found to be unable to reduce their prednisone dosage were started on methotrexate therapy with a dose range of 15 to 50 mg per week.³¹ They were treated for 18 months. Fifteen patients discontinued the regular use of prednisone, nine patients reduced prednisone by more than 50%, and one patient failed to respond. The FEV-1's improved from 1.7 to 1.9. The subjective scores all improved. Adverse drug reactions were mild and did not lead to discontinuation of drug therapy. The authors conclude that methotrexate is effective and safe when used as a long-term corticosteroid sparing agent in patients with severe bronchial asthma.

Almitrine bismesylate is a peripheral chemoreceptor agonist that has been found to improve PO₂ and PCO₂ in patients with hypoxemic chronic obstructive pulmonary disease when administered either intravenously or orally. The drug has been in trials in Europe, and patients have shown improvement in PO₂ that was maintained without developing tolerance. The studies have also shown that the increase in PO₂ is out of proportion to changes in ventilation, suggesting that almitrine bismesylate decreases the degree of ventilation-perfusion inequality in the lung. Watanabe et al³² studied the long-term effect of almitrine bismesylate in 25 patients with COPD and moderate hypoxemia residing at an altitude of 1,500 meters. They confirmed that the drug causes a long-term improvement in arterial oxygenation in hypoxemic patients with COPD who reside at altitude. Lower doses of the drug might have produced the same effect without the side effect of

weight loss seen in 5 of 13 patients, and peripheral paresthesias of the lower extremities seen in 3 patients. This is exciting because the drug offers a new therapeutic modality for patients with COPD. In some patients, it may reduce or eliminate the need for oxygen.

Vascular and Interstitial Disease

Yellin et al reviewed 63 patients with superior vena cava syndrome to determine whether they received clinical relief with therapy.³³ In this series, 47% of the patients had bronchogenic carcinoma and another 20% had lymphoma. In 43 cases, the superior vena cava syndrome was the presenting symptom of a mediastinal condition. Forty-one patients underwent diagnostic procedures with no major complications and diagnosis was obtained in 36. Six patients had surgical treatment, 45 had radiation, chemotherapy, or both. There was no mortality directly associated with venous congestion. Yellen et al conclude that symptomatic relief occurred in 80% of treated patients and that superior vena cava syndrome should not, per se, be feared. Second, they felt accurate diagnosis can be achieved with minimal morbidity.

Goldhaber³⁴ has reviewed the role of thrombolysis in venous thromboembolism. He discusses various reasons for the lag in advances in thrombolytic treatment for pulmonary embolism and deep venous thrombosis. Available thrombolytic therapy has not gained widespread acceptance because the risk is perceived to outweigh the benefits. He describes two novel recombinant tissue-type plasminogen-activator regimens for pulmonary embolism that are now being investigated. Optimal dosing regimens for pulmonary embolus and venous thrombosis must yet be de-

termined. The goal will be to develop the best possible thrombolytic dosing regimens in large clinical trials and determine which patients with pulmonary embolism and deep venous thrombosis will benefit the most from thrombolysis followed by anticoagulation, rather than anticoagulation alone. Goldhaber emphasizes that this expensive and potentially risky therapy for pulmonary vascular disease will not gain widespread application unless sufficient time and resources are invested in properly designed and conducted clinical trials.

Tazelaar et al³⁵ reviewed open lung biopsies from 14 patients and autopsied tissue from a patient with polymyositis/dermatomyositis. They attempted to correlate histologic features with clinical, radiographic and prognostic variables. Some patients had bronchiolitis obliterans organizing pneumonia; some had interstitial pneumonia; others had diffuse alveolar damage. The patients with bronchiolitis obliterans organizing pneumonia had a more favorable prognosis, and those with diffuse alveolar damage had a uniformly poor prognosis. The authors conclude that there is a broad range of histologic findings in the lung disease associated with polymyositis/dermatomyositis, and that subclassification may be a useful predictor for prognosis.

Schwartz et al³⁶ reviewed the clinical significance of asbestos-induced pleural fibrosis, comparing the relationship between radiographic evidence of pleural fibrosis and spirometric values in 1,211 sheet-metal workers. This study showed that both circumscribed plaques and diffuse pleural thickening were independently associated with decrements in FVC, but not in the FEV-1/FVC ratio. Furthermore, the

data indicate that the effect of diffuse pleural thickening on decrements in FVC is approximately twice as great as that seen with circumscribed pleural plaques. The presence and type of pleural fibrosis among asbestos-exposed workers was independently associated with a pattern of spirometry that suggests an underlying restrictive defect in lung function.

References

- ¹ Rommens JM, Iannuzzi MC, Kerem BS, et al: Identification of the Cystic Fibrosis Gene: Chromosome Walking and Jumping. *Science* 245, No 4922, 1059-1065. Sept 8, 1989.
- ² Riordan JR, Rommens JM, Kerem BS, et al: Identification of the Cystic Fibrosis Gene: Cloning and Characterization of Complementary DNA. *Science* 245, No 4922, 1066-1073. Sept 8, 1989.
- ³ Kerem BS, Rommens JM, Buchanan JA, et al: Identification of the Cystic Fibrosis Gene: Genetic Analysis. *Science* 245, No 4922, 1073-1080. Sept 8, 1989.
- ⁴ Cohn DL, Catlin BJ, Peterson KL, et al: A Sixty-two Dose, Six-month Therapy for Pulmonary and Extra-pulmonary Tuberculosis. *Ann Int Med*, 112:407-415. 1990.
- ⁵ Combs DL, O'Brien RJ, Geiter LJ; US Public Health Service Tuberculosis Short-course Chemotherapy Trial 21: Effectiveness, Toxicity, and Acceptability. The report of the final results. *Ann Int Med*, 112:397-406. 1990.
- ⁶ Iseman MD, Madsen L, Goble M, Pomerantz M: Surgical Intervention in the Treatment of Pulmonary Disease Caused by Drug-Resistant Mycobacterium Tuberculosis. *Am Rev Resp Dis*, 141:623-625. 1990.
- ⁷ O'Brien RJ, Geiter LJ, and Lyle MA: Rifabutin for the Treatment of Pulmonary Mycobacterium Avium Complex. *Am Rev Res Dis*, No 4, 141:821-826. April, 1990.
- ⁸ Simonds AK, Newman SP, Johnson MA, et al: Alveolar Targeting of Aerosol Pentamidine. *Am Rev Resp Dis*, 141:827-829. April, 1990.
- ⁹ Stover DE, Greeno RA, Gagliardi AJ: The Use of a Simple Exercise Test for the Diagnosis of Pneumocystis Carinii Pneumonia in Patients with AIDS. *Am Rev Resp Dis*, 139:1343-1346. 1989.
- ¹⁰ D'Alonzo GE, Smolensky MH, Feldman S, et al: Twenty-four Hour Lung Function in Adult Patients with Asthma. *Am Rev Resp Dis*, 142:84-90. 1990.
- ¹¹ Weiss KB: Seasonal Trends in US Asthma Hospitalizations and Mortality. *JAMA*, 263:2323-2328. May 2, 1990.
- ¹² Pauli BD, Reid RL, Munt PW, et al: Influence of the Menstrual Cycle and Airway Function on Asthmatic and Normal Subjects. *Am Rev Resp Dis*, 140:358-362. August, 1989.
- ¹³ Petty TL: The National Mucolytic Study (Results of a randomized, double blind placebo-controlled study of iodinated glycerol in chronic obstructive bronchitis). *Chest*, 97:75-83. 1990.
- ¹⁴ Gong H, Jr: Advising Pulmonary Patients about Commercial Air Travel. *J Resp Dis*, No 5, 11:484-499. May, 1990.
- ¹⁵ Tran DD, Groeneveld ABJ, Van der Meulen J et al: Age, Chronic Disease, Sepsis, Organ System Failure, and Mortality in a Medical Intensive Care Unit. *Critical Care Medicine*, 18:474-479. May, 1990.
- ¹⁶ Dark DS, Pingleton SK: Non-hemorrhagic Gastrointestinal Complications in Acute Respiratory Failure. *Crit Car Med*, 17:755-758. Aug, 1989.
- ¹⁷ Brinson RR, Pitts WM: Gastrointestinal Complications of Acute Respiratory Failure. *Crit Car Med*, 17:841-842. Aug, 1989.
- ¹⁸ Brochard L, Harf A, Lorino H, Lemaire F; Inspiratory Pressure-Support Prevents Diaphragmatic Fatigue During Weaning from Mechanical Ventilation. *Am Rev Resp Dis*, 139:513-521. 1989.
- ¹⁹ Lain DC, Chaudhary BA, Thorarinsson B, Speir WA, Jr: Auto-PEEP and Proximal Airway Pressure. *Chest* No 4:97:771. April, 1990.
- ²⁰ Hoffman R, Agatston A, Krieger B: Cheyne-Stokes Respiration in Patients Recovering from Acute Cardiogenic Pulmonary Edema. *Chest*, February, 97:410-412. 1990.
- ²¹ Hanley PJ, Miller TW, Steljes DG, et al: The Effect of Oxygen on Respiration and Sleep in Patients with Congestive Heart Failure. *Ann of Int Med*, 111:777-782. Nov 15, 1989.
- ²² Peters JI, Bell RC, Prihoda TJ, et al: Clinical Determinants of Abnormalities in Pulmonary Functions in Survivors of the Adult Respiratory Distress Syndrome. *Am Rev Resp Dis*, 139:1163-1168. 1989.
- ²³ Burkey P, Bodey GP: Nocardial Infection in Patients with Neoplastic Disease. *Rev of Inf Dis*, 1989; 11:407-412. May/June, 1989.
- ²⁴ Rickles FR: Thrombosis and Lung Cancer. *Am Rev Resp Dis*, No 3, 140:573-574. Sept, 1989.
- ²⁵ Minna JD: Genetic Events in the Pathogenesis of Lung Cancer. *Chest*, 96 No 1 Supplement, pgs 17S-21S. July, 1989.
- ²⁶ Katz RN: The Role of Antihistamines in Asthma Therapy. *J of Resp Dis*, No 4, 11:S17-S21. April, 1990.
- ²⁷ Tinkleman DG, Bucholtz GA, Kemp JP, et al: Evaluation of the Safety and Efficacy of Multiple Doses of Azelastine to Adult Patients with Bronchial Asthma Over Time. *Am Rev Resp Dis*, 141:569-574. 1990.
- ²⁸ North American Tilade Study Group: A Double Blind Multi-Center Group Comparative Study of the Efficacy and Safety of Nedocromil Sodium in the Management of Asthma. *Chest*, 97:1299-1306 1990.
- ²⁹ Kronenberger H, Kullmer T, Schultze-Werninghaus G: The Bronchodilatory Effect of Formoterol in Healthy Smokers and Non-Smokers. *Am Rev Resp Dis*, No 4, 141:A469. April, 1990.
- ³⁰ Salmeron S, Guerin JC, Godard P, et al: High Doses of Inhaled Corticosteroids in Unstable Chronic Asthma. *Am Rev Resp Dis*, 140:167-171. 1989.
- ³¹ Mullarkey MF, Lammert JK, Blumenstein BA: Long-term Metho-trexate Treatment in Corticosteroid-Dependent Asthma. *Ann Int Med*, 112:577-581. 1990.
- ³² Watanabe S, Kanner RE, Cutillo AG, et al: Long-term Effect of Almitrine Besmesylate in Patients with Hypoxemic Chronic Obstructive Pulmonary Disease. *Am Rev Resp Dis*, 140:1269-1273. 1989.
- ³³ Yellen A, Rosen A, Reichert N, Lieberman Y: Superior Vena Cava Syndrome. *Am Rev Resp Dis*, 141:1114-1118. 1990.
- ³⁴ Goldhaber SZ: Thrombolysis in Venous Thrombo-Embolism. *Chest*, vol 4, 97 supplement, pgs 176S-181S. April, 1990.
- ³⁵ Tazelaar HD, Viggiano RW, Pickersgill J, Colby RV: Interstitial Lung Disease in Polymyositis and Dermatomyositis. *Am Rev Resp Dis*, 141:727-733. 1990.
- ³⁶ Schwartz DA, Fuortes LJ, Galvin JR, et al: Asbestos-induced Pleural Fibrosis and Impaired Lung Function. *Am Rev Resp Dis*, 141:321-326. 1990.

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Recent Advances in Hematology

James P. Crowley, MD

A major advance . . . in allogeneic marrow transplantation has been the development of a National Bone Marrow Registry of non-related HLA-matched donors . . .

Hematology is the specialty of medicine that is concerned with the diagnosis and treatment of abnormally low or high levels of blood cells, bleeding and clotting disorders, and the treatment of leukemia and related malignancies. Hematologists use treatments which alter the many functions mediated by the blood and these treatments have found a broad range of application to hematologic diseases as well as diseases arising in other organs. These treatments include various forms of immunotherapy, the selective removal of pathologically altered blood constituents, the transfusion of highly purified blood products and components, and bone marrow transplantation.

The present review will highlight some of the remarkable advances in the field that have occurred in the last few years (Table

1). Some of these new methods of diagnosis and treatment have been recently introduced in Rhode Island and others will shortly be introduced so this review should be particularly relevant for physicians in Rhode Island at this time.

Hematopoietic Growth Factors

HGFs are glycoproteins that regulate both the proliferation and differentiation of the bone mar-

row progenitor cells.¹⁻³ HGFs have a dual role in stimulating both proliferation as well as differentiation. These factors by their direct action on cells constitutively bearing appropriate receptors, as well as by the indirect action of inducing receptors for other HGFs, regulate and control hematopoiesis. At present there are six promising HGFs for which clinical trials have been initiated.

ABBREVIATIONS USED:

AF: atrial fibrillation
AML: acute myelogenous leukemia
ALL: acute lymphocytic leukemia
CML: chronic myelogenous leukemia
DDAVP: desmopressin
DIC: disseminated intravascular coagulation
DNA: deoxyribonucleic acid
EPO: erythropoietin
FDA: Food & Drug Administration
G-CSF: granulocyte colony stimulating factor
GM-CSF: granulocyte-monocyte colony stimulating factor

GVH: graft versus host
HDIVIG: high dose intravenous gamma globulin
HGF: hematopoietic growth factors
HLA: human leukocyte antigen
IgG/A: immune globulin G, A
IL: interleukin
ITP: immune thrombocytopenia purpura
M-CSF: monocyte colony stimulating factor
mRNA: messenger ribose nucleic acid
PMN: polymorphonuclear (leukocyte)
RES: reticulo-endothelial system
SLE: systemic lupus erythematosus
TSA: tumor specific antigens

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Some of the different applications of these factors is shown in Table 2.

Erythropoietin

Erythropoietin (EPO), the first discovered of the human growth factors (HGF), was also first to be licensed by the FDA for clinical use in 1989. Goldwasser and his associates extracted about 1 mg of this substance from tens of thousands of gallons of urine from patients with severe anemia. This painstaking work paved the way for the later elucidation of EPO's structure and eventual biosynthesis using recombinant DNA technology.⁴ Clinical investigators interested in the anemia of progressive renal failure pioneered treatment with EPO.⁵ There are approximately 80,000 people undergoing chronic renal dialysis in the United States, and several studies suggest that most of these patients are anemic. Fifteen per cent of all patients in Rhode Island on long-term dialysis required greater than ten transfusions annually, and the mortality in these patients was more than twice that of the untransfused group.⁶ Eschbach et al have shown that in every patient with chronic renal failure studied, the anemia responded to erythropoietin provided a sufficient dose was used.⁵ The application of erythropoietin to the anemia of long-term dialysis and chronic renal failure has provided the most substantial benefit of HGFs to patients to date. Other successful applications of EPO therapy are listed in Table 3.^{7, 8}

Other Marrow Growth Factors

Two HGFs are known to raise the polymorphonuclear leukocyte (PMN) count, critical for defense against infection. GM-CSF acts relatively early in the cell hierarchy and induces differentiation of multiple lineages including

Table 1. Some Recent Advances in Clinical Hematology

1. Erythropoietin and hematopoietic growth factors for marrow failure
2. Bone marrow transplantation for leukemia and related disorders
3. Detection of residual leukemia by PCR^o and RFLP^{*}
4. Polyclonal IgG therapy for autoimmune disease and monoclonal therapy for cancer
5. Diagnosis, treatment, and prevention of hypercoagulability
6. Autologous donation and blood conservation
7. Educational interactive videodiscs for blood and marrow morphology

^oPolymerase chain reaction amplification of oncogene m-RNA

^{*}Restriction fragment length DNA polymorphisms

PMNs, monocytes, and eosinophils.¹⁻³ G-CSF affects more differentiated precursors. Patients with myeloid leukemia may express receptors for these growth factors⁹ and so there has been concern about the use of these factors to treat patients with leukemia and the related disorders.⁹ Also, GM-CSF activates the PMNs. Activation causes the PMN to be more adhesive and concerns have been raised about the possibility of adhesive PMNs being sequestered in the lung and aggravating inflammation.¹⁰ G-CSF raises the PMN level but does not activate PMNs.

Interleukin 3 (Multi-CSF) is a glycoprotein HGF that affects an early stage of hematopoiesis and increases in vitro the production of colonies that have erythroid, granulocytic, monocytic and megakaryocytic properties.² Accordingly, interest in this agent as a treatment for aplastic anemia has arisen.⁹ IL-3 has been used in conjunction with other agents such as G-CSF and GM-CSF in an effort to produce a combination

HGF therapy that would both cause the stem cell population to proliferate and become susceptible to further differentiation and proliferation.⁹ M-CSF activates monocytes to kill fungi, and IL-6 increases platelet production in animals. Preliminary studies in humans are underway.

Bone Marrow Transplantation

Thomas and co-workers first attempted marrow transplants in humans in the 1950s. However, early experience with transplantation was dismal, and all but twin transplants succumbed to a severe reaction in which the engrafted bone marrow graft attacked the host (GVH). The development in the 1960s of typing sera for the human histocompatibility loci, HLA-A and -B, and later other histocompatibility loci determinants including HLA, -C, -D and -DR, resulted in reduced GVH and increased success in the treatment of aplastic anemia, acute leukemia, and lymphoma.¹¹⁻¹⁴

Allogeneic bone marrow trans-

Table 2. Clinical Application of Recombinant Growth Factors

EPO	Anemia
G-CSF	Neutropenia
GM-CSF	Neutropenia
	Monocytopenia
	Immunosuppression*
M-CSF	Monocytopenia*
	Immunosuppression*
IL-3 (multi-CSF)	Aplastic anemia (with other factors)
IL-6	Thrombocytopenia*

*Application mainly supported by animal studies

Table 3. Current Applications of Recombinant Human Erythropoietin to Anemia

Renal failure and long-term dialysis
Anemia of chronic disease
Anemia of malignancy
Preoperative autologous donation before surgery
Perioperative management of surgical patients
Hypoplastic anemia
Myelodysplasia
Enhanced recovery following bone marrow transplantation
Hemoglobinopathy

plantation is now applied in several diseases listed in Table 4.¹¹⁻¹⁴ Allogeneic bone marrow transplantation is the only treatment able to permanently eradicate the leukemic clone in chronic myelogenous leukemia.¹⁴ Application of bone marrow transplantation to CML has resulted in improved possibilities for cure in this disorder. Recent results from Seattle (ED Thomas, personal communication) have indicated that up to 95% of CML patients may be successfully transplanted if the transplant is performed during the first year following diagnosis. A major advance that has led to an upsurge in allogeneic marrow transplantation¹⁴ has been the development of a National Bone Marrow Registry of non-related HLA-matched donors (to access, phone 1-800-950-1050) which has greatly increased the possibility of finding a donor when no sibling match is available.

Autologous bone marrow transplantation requires the infusion of the patient's own marrow as opposed to that of a matched sib-

ling donor. Unlike allogeneic bone marrow transplantation, the issues of donor availability and graft versus host disease are not relevant. Autologous bone marrow transplantation appears to be at present less efficacious than allogeneic transplantation for leukemia and lymphoma.¹⁵⁻²¹ With solid tumors, response rates have varied from 30% in gliomas up to 80% in breast cancer.^{18, 19} Unlike leukemias and lymphomas treated with autologous bone marrow transplantation, responses to autologous transplantation in solid tumours are relatively brief. Nevertheless, occasional long-term survivors have been demonstrated, and autologous marrow transplantation for solid tumours is being vigorously investigated.¹⁹

Detection of Residual Leukemia (Mixed Chimaerism)

Traditionally, residual leukemic cells following chemotherapy or bone marrow transplantation have been detected using morphologic techniques. In CML, Philadelphia

chromosome which is a reciprocal translocation between chromosomes 9 and 22 bears a human proto oncogene c-ABL normally located on chromosome 9. This oncogene is activated when it is translocated to the middle of the BCR gene region located on chromosome 22.²² Fusion produces a new gene expression which results in a new mRNA species. The ability to detect BCR/ABL chimaeric mRNA has recently been greatly enhanced by the application of the polymerase chain reaction which can detect extremely low levels of mRNA.²² When the oncogene or its product are unknown, DNA restriction fragment polymorphism (RFLP analysis) has emerged as the method of choice for studying chimaerism.¹¹ Leukemic chimaerism is often compatible with very long-term disease-free survival. Remarkably, the leukemic clone may persist then eventually disappear up to a decade after transplantation^{11, 22} indicating the existence of some as yet to be elucidated natural mechanism for the eradication of leukemia.

Immunoglobulin Therapy

Gamma globulins are quantitatively the most important constituent of the plasma proteins following albumin. Gamma globulins constitute a major defense against infection.²³ Patients with deficiencies are prone to a variety of infections caused by bacteria, viruses, and fungi. These patients have a higher than expected incidence of malignancies and autoimmune diseases.²⁴ Replacement of deficient immunoglobulin production by intravenous IgG has been shown to be efficacious in the reduction of infection.^{23, 25} High-dose intravenous gamma globulin (HDIVIG) can temporarily block the RES system,²⁶ and it has proven useful in the treatment of idiopathic thrombocyto-

Table 4. Applications of Bone Marrow Transplantation⁺ to Human Disease

Aplastic Anemia
Acute myelogenous and lymphoblastic leukemia
Chronic myelogenous leukemia
Immunodeficiency syndromes
Myelodysplasia
Hodgkin's disease and other lymphomas
Solid tumors including breast cancer ^o
Hemoglobinopathy

⁺ Allogeneic = matched sibling or matched unrelated donor

^oAutologous = person's own

penic purpura (ITP).²³ Other applications are shown in Table 5. HDIVIG does not transmit viral disease, and the incidence of allergic reactions is very low except in patients with concomitant IgA deficiency and anti-IgA antibodies.

These patients (with immunoglobulin deficiencies) have a higher than expected incidence of malignancies and autoimmune diseases.

Presently available immunoglobulin concentrates are polyclonal. Following the initial discovery of monoclonal antibodies in the mid 1970s,²⁷ several biotechnology enterprises fueled by investments from venture capitalists aimed at developing "magic bullets" for the treatment of cancer utilizing monoclonal antibodies directed against tumor-specific antigens (TSA).²⁸ Monoclonal antibodies to TSA have been conjugated to highly toxic substances such as ricin.²⁹ Phase I studies of ricin conjugates in solid tumors have included ovarian, breast, and colon cancer.^{27, 29} Unfortunately, few long-lasting responses have been observed. Monoclonal antibodies directed against leukemic-specific antigens in both AML and ALL are promising agents to cleanse bone marrow of residual leukemia cells in relapsed patients receiving autologous bone marrow transplantation.^{16, 21}

Advances in Coagulation

The development of desmopressin (DDAVP) which raises FVIII and thereby enhances platelet function is a real advance in the nontransfusional treatment of congenital and acquired bleeding disorders.³⁰ DDAVP has largely re-

Table 5. Immunoglobulin Therapy

1. Patients with recurrent infections
2. Immune thrombocytopenia purpura (ITP)
3. Autoimmune neutropenia, hemolytic anemia, and pure red cell aplasia
4. Kawasaki syndrome
5. Myasthenia gravis, SLE, and related autoimmune disorders
6. Relapsing polyneuropathy
7. Acquired inhibitors of coagulation
8. Monoclonal purging of autologous bone marrow
9. Treatment of solid tumors
10. Selected patients with acquired immunodeficiency syndromes

placed transfusional therapy in patients with mild hemophilia and heterozygous von Willebrand disease.³⁰ DDAVP has also been shown to be effective in reducing the bleeding time in uremia, cirrhosis, and congenital and acquired platelet storage pool deficiency.³⁰

Aspirin (Table 6) which inactivates platelets by inhibiting thromboxane synthesis has found clinical application in the prevention of arterial and venous thromboembolism.³¹ Prophylactic aspirin administration is effective in the secondary prevention of myocardial infarction, death in unstable angina, and in the prevention of early graft occlusion following coronary artery bypass grafting.³² Prophylactic aspirin has also been found to be efficacious in the prevention of stroke and death in patients with transient ischemic attacks³¹ and for patients with atrial fibrillation (AF) unrelated to valvular heart disease who have a risk of ischemic stroke which is 5 times higher than that of persons with normal sinus rhythm. Administration of daily aspirin to AF patients resulted in a stroke rate which was approximately half of that of patients given placebo.³³ Some authorities on thrombosis have suggested that intermittent aspirin dosage may be superior to daily use.^{31, 32} The inactivation of platelets by aspirin is known to be relatively long lasting while the inactivation of endothelial production of

platelet inhibitory prostacyclin is transient. Intermittent administration of aspirin might well allow endothelial prostacyclin production to recover while a direct antiplatelet effect could still continue.

The indications for full dose warfarin therapy to prevent recurrence of previously established thrombi are established, but use of low doses of warfarin to prevent new thrombi has not received much attention. A recent study of patients at high risk for thrombosis because of indwelling central venous catheters has shown that at a dose of 1 mg of warfarin daily there was a highly significant reduction in thrombosis.³⁴ This approach may be applicable to other groups of patients at high risk for thrombosis. A recent Norwegian study has shown that prophylactic anticoagulation therapy appears to be effective in reducing the risk of fatal and non-fatal recurrent coronary as well as cerebral arterial thrombosis in patients with prior myocardial infarction.³⁵

The mechanisms of hypercoagulability have become better understood in recent years.³⁶ The elucidation of the structure of the vitamin K-dependent factors, Protein C and S, have allowed for the development of immunological and functional assays for these inhibitors of blood coagulation.³⁶ Many familial cases of hypercoagulability are related to deficiencies of Protein C and Protein S.³⁶

Table 6. Thrombotic Conditions in Which Prophylactic Aspirin Provides Significant Benefit

Myocardial infarction
Unstable angina
Prevention of graft occlusion after coronary artery bypass graft
Stroke from atrial fibrillation (both rheumatic and non-rheumatic)

Acquired Protein S deficiency has been observed in patients with liver disease, DIC, nephrotic syndrome, pregnancy,³⁷ and inflammatory bowel disease.³⁸

A study in Rhode Island showed that patients with thalassemia minor have less than the expected incidence of myocardial infarction.

Even in those patients with significant predisposing coagulation abnormalities such as congenital heterozygous Protein C and Protein S deficiency, most will not experience thrombosis.³⁶ Other factors which lead to hypercoagulability need to be identified. An important cause of hypercoagulability is the lupus anticoagulant, antiphospholipid autoantibodies that are found in patients with SLE and which are frequently associated with otherwise unexplained venous and arterial thrombosis^{37, 39, 40} and recurrent first and second trimester fetal abortions³⁷ in patients with no evidence of SLE. The syndrome of heparin-induced thrombocytopenia with thrombosis continues to be increasingly recognized as a factor paradoxically predisposing to thrombosis. A patient with heparin-induced thrombocytopenia was recently shown to respond well to treatment with high dose intravenous gammaglobulin.⁴¹ A study in Rhode Island showed that patients with thalassemia minor have less than the expected incidence of myocardial infarction.⁴² A recent experimental study

has shown that higher hematocrits may promote the net accumulation of thrombosis.⁴³ More study of the effect of blood cells on viscosity and hematocrit, and their relation to hypercoagulability is clearly needed.

Advances in Transfusion Medicine and Education

Recent data show that physician education in more appropriate transfusion practices has reduced the inappropriate use of blood components.⁴⁴ The use of erythropoietin (EPO) in conjunction with autotransfusion⁴⁵ and predeposit autologous donation⁸ has further contributed to a reduction in inappropriate blood product use and consequently a reduction in disease transmission and reactions. Transfusion-associated acquired immunodeficiency syndrome (AIDS) remains a major concern.⁴⁶ This risk has been reduced because of testing of donor units for HIV. The current estimated risk of HIV transmission from blood transfusion in Rhode Island is approximately one in one hundred thousand (Dr R. Yankee, personal communication). Nevertheless, about 20% of all transfusions will still result in some type of adverse effect.⁴⁷ Fortunately, recent introduction of the test for hepatitis C should reduce the most serious risk of blood transfusion, transfusion-associated viral hepatitis, by approximately 80%.⁴⁷

The teaching of transfusion medicine, of coagulation, and especially of the diagnostic interpretation of blood and bone marrow, has been enhanced by the

recent development of a comprehensive laser videodisc which incorporates most of the teaching slides of blood and bone marrow in the collection of the American Society of Hematology.⁴⁸ This development should open the way toward highly individualized and effective computer interactive videodisc instruction in hematology.⁴⁹

Summary

Erythropoietin and other recombinant hematopoietic growth factors for the treatment of marrow failure has been a major recent advance in hematology. Genetic engineering technologies are replacing more empirical methods for the detection and treatment of hematologic disease. Bone marrow transplantation is a more effective means of cure than chemotherapy for many patients with acute leukemia and related diseases. Autologous marrow transplantation is increasingly applied in the treatment of solid tumors. Intravenous gamma globulin has been found to be effective in selected patients with steroid unresponsive autoimmune hematologic disease as well as nonhematologic autoimmune disorders. Advances in knowledge of the natural anticoagulants have elucidated the pathogenesis of many cases of recurrent venous and arterial thromboses. The lupus anticoagulant has emerged as a marker for many patients who are hypercoagulable. It has been increasingly recognized that transfusions are unnecessary in many situations in which transfusions were formerly routine. Computer interactive laser videodisc technology has improved the teaching of morphologic diagnosis of hematologic disease. The provision of these sometimes expensive but often cost effective and superior modalities in an era of aggressive

cost containment will prove a worthy challenge to the Rhode Island medical community in coming years.

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References

- Groopman JE, Molina J-M, Scadden DT: Hematopoietic growth factors: Biology and clinical applications. *N Engl J Med*, 321:1449-1459, 1989.
- Mazur E: The basic concepts of hematopoiesis and the hematopoietic growth factors. *Clin Pharmacol Ther*, 46:250-256, 1989.
- Cannistra SA, Griffin JD: Regulation of the production and function of granulocytes and monocytes. *Semin Hematol*, 25:173-188, 1988.
- Bunn HF: Recombinant erythropoietin in cancer patients. *J Clin Oncol*, 8:949-951, 1990.
- Eschbach JW, et al: Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. *N Engl J Med*, 316:73-78, 1987.
- Crowley JP, Nealey TA, Metzger J, Pono L, Chazan JA: Transfusion and long-term hemodialysis. *Arch Intern Med*, 147:1925-1928, 1987.
- Miller CB, et al: Decreased erythropoietin response in patients with the anemia of cancer. *N Engl J Med*, 322:1689-92, 1990.
- Goodnough LT, Rudnick S, Price TH, Ballas S, Collins M, Crowley J, et al: Increased preoperative collection of autologous blood with recombinant human erythropoietin therapy. *N Engl J Med*, 321:1163-1168, 1989.
- Cheson BD: The myelodysplastic syndromes: Current approaches to therapy. *Ann Intern Med*, 112:932-941, 1990.
- Mayer P, et al: Recombinant human GM-CSF induces leukocytosis and activates peripheral blood polymorphonuclear neutrophils in nonhuman primates. *Blood*, 70:206-213, 1987.
- Petz LD: Immunohematologic problems associated with bone marrow transplantation. *Transf Med Rev*, 1(2):85-100, 1987.
- Appelbaum FR, et al: Bone marrow transplantation for patients with myelodysplasia. *Ann Intern Med*, 112:590-597, 1990.
- Wingard JR, et al: Allogeneic bone marrow transplantation for patients with high-risk acute lymphoblastic leukemia. *J Clin Oncol*, 8:820-830, 1990.
- McGlave PB, et al: Therapy for chronic myelogenous leukemia with unrelated donor bone marrow transplantation: Results in 102 cases. *Blood*, 75:1728-1732, 1990.
- Freedman AS, et al: Autologous bone marrow transplantation in B-cell non-Hodgkin's lymphoma: Very low treatment-related mortality in 100 patients in sensitive relapse. *J Clin Oncol*, 8:784-791, 1990.
- Gorin NC, et al: Autologous bone marrow transplantation for acute myelocytic leukemia in first remission: A European Survey of the role of marrow purging. *Blood*, 75:1606-1614, 1990.
- Petersen FB, et al: Autologous marrow transplantation for malignant lymphoma: A report of 101 cases from Seattle. *J Clin Oncol*, 8:638-647, 1990.
- Armitage JO: Bone marrow autotransplantation. *Am J Med*, 86:203-206, 1989.
- Cheson BD, et al: Autologous bone marrow transplantation. *Ann Intern Med*, 110:51-65, 1989.
- ASCO/ASH Recommended criteria for the performance of bone marrow transplantation. *Blood*, 75:1209, 1990.
- Ball ED, et al: Autologous bone marrow transplantation for acute myeloid leukemia using monoclonal antibody-purged bone marrow. *Blood*, 75:1199-1206, 1990.
- Epner DE, Koeffler HP: Molecular genetic advances in chronic myelogenous leukemia. *Ann Intern Med*, 113:3-6, 1990.
- Nelson JM: Intravenous immunoglobulin: Silver bullet of the 80's. *Lab Med*, 19:799-805, 1988.
- Cooperative Group for the Study of Immunoglobulin in Chronic Lymphocytic Leukemia: Intravenous immunoglobulin for the prevention of infection in chronic lymphocytic leukemia. *N Engl J Med*, 319:902-7, 1988.
- Schur PH: IgG subclasses — a review. *Ann Allergy*, 58:89-99, 1987.
- Basta M, et al: Mechanism of therapeutic effect of high dose intravenous immunoglobulin. *J Clin Invest*, 84:1974-1981, 1989.
- Salmon SE: Monoclonal antibody immunoconjugates for cancer. *Antibody. Immunoconjugates, and Radiopharmaceuticals*, 2:63-70, 1989.
- Teitelman R: *Gene Dreams, Wallstreet, Academia and the Rise of Biotechnology*, Basic Books, New York, 1989.
- Dillman RO: Monoclonal antibodies for treating cancer. *Ann Intern Med*, 111:592-603, 1989.
- Mannucci PM: Desmopressin: A nontransfusional form of treatment for congenital and acquired bleeding disorders. *Blood*, 72:1449-1455, 1988.
- O'Brien JR: Perspective on antiplatelet drugs. *Semin Thromb Hemost*, 15:171-172, 1989.
- Reilly IAG, Fitzgerald GA: Aspirin in cardiovascular disease. *Drugs*, 35:154-176, 1988.
- Study Group Investigators: Preliminary report of stroke prevention in atrial fibrillation study. *N Engl J Med*, 322:863-868, 1990.
- Bern MM, et al: Very low doses of warfarin can prevent thrombosis in central venous catheters. *Ann Intern Med*, 112:423-428, 1990.
- Smith P, Arnesen H, Holme I: The effect of warfarin on mortality and reinfarction after myocardial infarction. *N Engl J Med*, 323:147-152, 1990.
- Rick ME: Protein C and Protein S: Vitamin K-dependent inhibitors of blood coagulation. *JAMA*, 263:701-703, 1990.
- Crowley JP: Coagulopathy and bleeding in the parturient patient. *RI Med J*, 72:135-143, 1989.
- Wyshock E, Caldwell M, Crowley JP: Deep venous thrombosis, inflammatory bowel disease, and Protein S deficiency. *Am J Clin Pathol*, 90:633-635, 1988.
- Lechner K: Lupus anticoagulant and thrombosis. *Thromb Haemost*, 21:525-547, 1987.
- Love PE, Santoro SA: Antiphospholipid antibodies: anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and in non-SLE disorders. *Ann Intern Med*, 112:682-698, 1990.
- Frame JN, et al: Correction of severe heparin-associated thrombocytopenia with intravenous immunoglobulin. *Ann Intern Med*, 111:946-947, 1989.
- Crowley JP, Sheth S, Capone RJ, Schilling RF: A paucity of thalassemia trait in Italian men with myocardial infarction. *Acta Haemat*, 78:249-251, 1987.
- Cadroy Y, Hanson SR: Effects of red blood cell concentration on hemostasis and thrombus formation in a primate model. *Blood*, 75:2185-2193, 1990.
- Crowley JP, Guadagnoli E, Pezzullo J, Fuller J, Yankee R: Changes in hospital component therapy in response to reduced availability of whole blood. *Transfusion*, 28:4-7, 1988.
- Levine EA, et al: Perioperative recombinant human erythropoietin. *Surgery*, 106:432-438, 1989.
- Mayer K: Transfusion of the patient with acquired immunodeficiency syndrome. *Arch Pathol Lab Med*, 114:295-297, 1990.
- Walker RH: Transfusion risks. *Am J Clin Pathol*, 88:374-378, 1987.
- Fine J, et al: Laboratory Medicine Vido Library: ASH Atla of Hematology. Univ. of Washington Health Sciences Center for Educational Resources, 1990.
- Crowley JP: Interactive Video Technology in Transfusion Medicine. In: Summers S, et al, eds. *Alternative Education Methods for Continuing Education*, AABB, 1987.

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Advances in Endocrinology and Metabolism 1989-1990

Preston Lamberton, MD

... large doses of insulin, often used to treat insulin resistant diabetic patients, may therefore be a risk factor for the development of coronary artery disease.

During the past year there have been a number of advances in the field of endocrinology and metabolism which either significantly advance our understanding of endocrine pathophysiology or modify and enhance our approach to the treatment of endocrine diseases.

Diabetes Mellitus

Diabetes mellitus is the most common disease in this field and certainly many of the noteworthy studies during this past year were in this area. The treatment of non-insulin dependent diabetes (type II DM) often involves a combination of diet, exercise, and oral hypoglycemic agents such as the sulfonylurea medications. In addition to the sulfonylurea agents, the biguanide metformin is frequently used in Europe to treat patients with type II DM. Metformin can be associated with an improvement in both hyperglycemia and with lipid abnormalities although its mechanism of

action remains unclear.¹ If and when this drug becomes available for therapeutic use in the United States, the health care professional will likely have a very effective medication to add to those already available for the treatment of type II DM. In terms of diabetic diets, protein restriction has received a lot of attention as a possible means of improving diabetic nephropathy. In a recent editorial, the potential risks and benefits of low-protein diets were reviewed.² It appears that low protein diets may slow the progression of established diabetic nephropathy, possibly postponing the need for dialysis. However, whether similar protein restricted diets can prevent the initial development of nephropathy is unknown, as are the possible long-term risks of a protein restricted diet.

In the area of endocrine immunology, the potential prevention of type I DM has been studied by numerous investigators. Type I, insulin dependent, diabetes is caused by the autoimmune destruction of pancreatic islet cells. Cyclosporine has therefore been studied as a means of interfering with this autoimmune islet cell destruction. In an investigation by

Bougneres and colleagues, it was shown that the treatment of children with type I diabetes, soon after diagnosis, reduced insulin dependence for up to one year in half the patients studied.³ Further studies will be necessary, however, to clarify whether immunosuppressive therapy will have a long-lasting effect to fully prevent the development of insulin dependent diabetes.

In the treatment of diabetes, two additional areas that continue to receive active investigation in-

ABBREVIATIONS USED:

ACTH: *adrenocorticotrophic hormone*

AIDS: *acquired immune deficiency disease*

DCCT: *Diabetes Control and Complications Trial*

DM: *diabetes mellitus*

FDA: *Food & Drug Administration*

FSH: *follicle stimulating hormone*

GI: *gastrointestinal*

HDL: *high density lipoprotein*

HIV: *human immune deficiency virus*

PTH: *parathyroid hormone*

TSH: *thyroid stimulating hormone*

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clude the use of artificial pancreatic devices and pancreatic transplantation. In a study by Sandek and his colleagues, it was demonstrated that patients could be successfully treated with a peritoneally implanted programmable insulin pump.⁴ The peritoneal site is potentially a very effective delivery site for insulin treatment since this route would mimic the endogenous secretion of insulin into the portal circulation. Still lacking, however, in the pump devices available is a glucose sensing mechanism that would allow a pump to match insulin delivery to ambient blood glucose concentrations. If and when a reliable and practical glucose sensing device is developed, it would appear that many diabetic patients could be candidates for treatment with an insulin pump device. Pancreatic transplantation has also been receiving increasing study as a means to potentially "cure" diabetes. In a study from Minnesota,⁵ it was demonstrated that successful pancreas transplantation in diabetic patients who previously had renal transplantation was associated with an improvement in the histological evidence of diabetic nephropathy in the transplanted kidneys. This important study not only demonstrated again the potential of pancreatic transplantation to cure diabetes but also provided evidence that normoglycemia (following successful pancreatic transplants) may help prevent certain diabetic complications.

The role of hyperglycemia and other factors potentially promoting the development of diabetic complications still needs further clarification. Several studies this past year^{6, 7} suggested that glycemic control and blood pressure may be two important factors which determine the development and course of dia-

betic retinopathy and nephropathy. However, there is still some disagreement about the potential value of tight diabetic control in reducing the rate of diabetic microvascular, neurological, and macrovascular complications. A large multicenter study, the Diabetes Control and Complications Trial (DCCT), is currently examining the question of whether intensive insulin therapy (to achieve near normoglycemia) can prevent the development of diabetic retinopathy. At present this study is partially completed and a preliminary report was recently published.⁸ Unfortunately, no data on the effect of diabetic control on retinopathy has been released as yet from the DCCT study but when the results are available, the findings will likely have a major effect on our approach to glucose control in the treatment of diabetes.

Recently attention has been directed at the possible relationship between hyperinsulinemia and atherosclerosis with an association being noted between elevated plasma insulin levels and coronary artery disease. A study in 1989⁹ demonstrated that patients with hyperinsulinemia and normal glucose tolerance have increased risk factors for coronary disease including elevated blood pressure levels, low HDL levels, and elevated triglycerides. This important finding demonstrates that elevated plasma insulin levels may be associated with abnormalities in lipid metabolism and blood pressure that could predispose patients to coronary artery disease. Of potential concern is that large doses of insulin, often used to treat insulin resistant diabetic patients, may therefore be a risk factor for the development of coronary artery disease. Certainly this association needs to be better defined but additional studies should be forthcoming hopefully clarifying

this important issue.

A study in 1989¹⁰ raises the question of whether patients with diabetes can be identified by elevated erythrocyte sodium-lithium countertransport measurements as predisposed to develop diabetic nephropathy. Erythrocyte sodium-lithium countertransport measurements are often elevated in patients with essential hypertension and may be a marker for the development of elevated blood pressure. It has been suggested that patients with diabetes who develop hypertension may have an increased risk of developing diabetic renal disease. Therefore, if normotensive diabetic patients could be identified by elevated erythrocyte sodium-lithium countertransport levels to be at increased risk of developing nephropathy, the countertransport determination could be valuable as an early marker of diabetic nephropathy. Carr and associates found that normotensive patients with type I diabetes and elevated sodium-lithium countertransport levels had increased glomerular filtration rates suggestive of early diabetic nephropathy. These investigators concluded that elevated sodium-lithium countertransport may be an early marker for the development of diabetic nephropathy.

Finally, one very important publication this past year was a position statement by the American Diabetes Association on a standards of care for the treatment of diabetes.¹¹ The diabetes standards of care, though perhaps somewhat controversial, do provide an excellent framework for the health care professionals to orient their approach to the care of patients with diabetes. The standards of care article covers the role of the initial evaluation of diabetic patients to confirm the diagnosis of diabetes, to review the treatment of the hypergly-

cemia, and to assess the patients for the presence of complications. Recommendations are then made for the continuing care of patients with diabetes, emphasizing such issues as frequency/type of laboratory testing, importance of foot care, and of periodic comprehensive eye examinations.

Hypoglycemia

At the opposite end of glucose metabolism, a study by Palardy and colleagues in 1989 demonstrated that patients suspected of having postprandial hypoglycemia infrequently have true hypoglycemia.¹² These investigators demonstrated that many patients with symptoms suggestive of hypoglycemia did not have low glucose levels when measurements were taken at the time of their symptoms. It was also suggested that glucose tolerance testing is not helpful in the diagnosis of hypoglycemia and the best way to establish a diagnosis of postprandial hypoglycemia is to document hypoglycemic glucose levels at the time patients have the symptoms suspected as due to hypoglycemia. It appears, however, that despite studies such as this, postprandial hypoglycemia will continue to be an over-diagnosed disorder.

Thyroid Disease

In the area of thyroid disease, an investigation by Fogelfeld and associates¹³ examined the recurrence rate of benign thyroid nodules after surgical removal in patients who had received radiation treatment to the head or neck. It was demonstrated that thyroid hormone administration after surgery reduces the risk of benign nodule recurrences, presumably through TSH suppression. These findings suggest that patients who undergo thyroidectomy for removal of benign thyroid nodules should be placed on thyroid hor-

mone suppression unless there are contraindications such as unstable coronary artery disease. In a study of Graves disease,¹⁴ the potential exacerbation of Graves' ophthalmopathy following radioactive iodide treatment of hyperthyroidism was examined. The results suggested that systemic corticosteroid treatment may prevent an exacerbation of the ocular changes in Graves' ophthalmopathy that may occur after I-131 treatment. It should be noted, however, that there is disagreement about whether I-131 treatment is actually associated with a worsening of Graves' ophthalmopathy. In another study involving hyperthyroid patients, Trzepacz and associates¹⁵ tried to determine if the elevations of thyroid hormone levels paralleled the degree of clinical hyperthyroidism. These investigators found that there was no particular correlation between the severity of the symptoms of hyperthyroidism and the degree of elevation of the free T4 index or total T3 levels. This study reflects the frequent clinical observation that patients with minimally elevated thyroid hormone levels may appear quite hyperthyroid while patients with marked laboratory abnormalities may appear less ill.

... patients with minimally elevated thyroid hormone levels may appear quite hyperthyroid while patients with marked laboratory abnormalities may appear less ill.

Osteoporosis

The treatment of established osteoporosis remains difficult, with limited therapeutic options. For years, estrogen has been used to treat women with postmenopausal osteoporosis, with older stud-

ies documenting a decline in fracture rate. The mechanism whereby estrogen improves calcium metabolism and bone loss has remained difficult to define. A study in 1989¹⁶ examined one possible mechanism of estrogen action, a resetting of the set point of PTH secretion. These investigators suggested that estrogen therapy may lead to a reduced secretion of PTH (and therefore less bone loss) by decreasing the level of serum calcium which triggers PTH secretion (ie, with estrogen therapy, a lower serum calcium would be necessary for PTH to be released). The results seem to provide one of the best explanations so far as to why estrogen treatment may lead to a reduced rate of bone loss. The effect of fluoride in the treatment of osteoporosis has also received considerable study and several publications from this past year yielded conflicting results on the benefits of sodium fluoride in patients with postmenopausal osteoporosis. Fluoride appears to stimulate new bone matrix and can potentially increase bone mass. However, sodium fluoride has been variably reported this past year as either being effective at improving bone mass in the spine,¹⁷ at reducing vertebral fracture rate,¹⁸ or as ineffective in the treatment of osteoporosis.¹⁹ In the latter study by Riggs and colleagues, fluoride did improve bone mass in the spine but decreased bone mass in the radius. The discrepant effects relate most likely to the types of bone present in the spine (cancellous) versus that present in the radius (cortical). In Riggs' study there was no improvement in the rate of spinal fractures after fluoride treatment. In several of the studies^{17, 19} there was a significant incidence of side effects from fluoride, mainly gastrointestinal and lower extremity pain. Thus the role of fluoride remains

to be defined in the treatment of osteoporosis. However, in a potentially very important study, Storm and associates²⁰ found that oral etidronate may be effective therapy for postmenopausal osteoporosis. These investigators demonstrated that etidronate given cyclically for 2 weeks, followed by a 13 week off-period over one year resulted in a significant decrease in the rate of vertebral fractures. If these results are confirmed, cyclical etidronate therapy may provide an excellent addition to our current regimen for the treatment of postmenopausal osteoporosis. Finally, an interesting observation by LaCroix and colleagues²¹ demonstrated that the use of thiazide diuretics may be associated with a reduced rate of hip fracture in men and women. One proposed mechanism for this finding involves the effects of thiazides at decreasing urinary calcium excretion and improving overall calcium balance.

Hypercalcemia of Malignancy

Hypercalcemia of malignancy occurs either because direct bone metastases cause release of calcium from involved bone or because a tumor-produced humoral factor causes diffusely increased bone breakdown. In the past, it was thought that certain solid tumors produced actual parathyroid hormone causing hypercalcemia through an ectopic PTH syndrome. However, closer investigation of patients with humoral hypercalcemia of malignancy revealed that true PTH is not the likely factor causing the hypercalcemia. Several recent studies, however, have demonstrated that patients with humoral hypercalcemia of malignancy may produce a parathyroid hormone-related protein with some amino acid homology to true PTH.^{22, 23} This important observation has led to the proposal that the para-

thyroid hormone-related proteins interact with PTH receptors in bone and kidney, causing the changes in calcium metabolism that result in hypercalcemia. These studies have provided considerable insight into the pathophysiology of humoral hypercalcemia of malignancy and suggest that measurements of the PTH-related proteins may be very helpful in the differential diagnosis of hypercalcemia (radioimmunoassays for these proteins are available in several research laboratories but are not yet commercially available).

... patients with humoral hypercalcemia of malignancy may produce a parathyroid hormone-related protein . . .

AIDS

The acquired immunodeficiency syndrome has been found to potentially result in a number of endocrine changes that may require treatment for optimal management of HIV infected patients. A recent study by Merenich and colleagues²⁴ suggests that early in the course of HIV infections, patients may develop mild endocrine dysfunction. These investigators noted laboratory evidence of subclinical abnormalities in serum cortisol responses to ACTH, free testosterone levels, and thyroid hormone parameters. These results suggest that patients with AIDS may have early involvement of a number of endocrine systems which if progressive could have an impact on the health of the patients. LoPresti and colleagues²⁵ studied the effects of AIDS on thyroid function tests in patients who had *P. carinii* pneumonia, some of whom did not survive the infection. It was found that non-sur-

vivors had lower T3 values than survivors. In addition reverse T3 levels were low in patients with AIDS-related complex and in outpatients with AIDS. Further as the AIDS syndrome progressed the investigators noted an increase in serum thyroid-binding globulin levels and total T4 levels. A review of these laboratory abnormalities suggests that the patients in this study were probably euthyroid but had alterations in thyroid test results that were correlated with the severity of their illness. According to the authors of this publication these laboratory abnormalities may be useful as a predictor of the outcome of the AIDS illness. Finally, an article by Aron in 1989 summarized the types of clinical endocrine dysfunction that may occur in patients with AIDS.²⁶ The author appropriately stresses the need to recognize and potentially treat abnormalities in endocrine function in those with HIV syndromes.

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Somatostatin

One of the most exciting new developments in endocrine therapy over the past several years involves the use of a somatostatin hormone analog in the treatment of a variety of endocrine (and non-endocrine) disorders. A number of recent publications involving the use of the somatostatin analogue have come from the research of Ivor Jackson and his colleagues at Rhode Island Hospital. In an excellent review published in 1989,²⁷ the possible

clinical applications of the somatostatin analogue were discussed. Somatostatin is a hormone synthesized in a number of tissues including the brain/hypothalamus, pancreas (D islet cells), and gastrointestinal tract. As a hormone, somatostatin tends to inhibit the release of other hormones (inhibits growth hormone release from the pituitary, for example). It is this action, as an inhibitor of various hormone systems, that has provided the basis for the use of the somatostatin analogue in the treatment of acromegaly, carcinoid tumors, and islet cell tumors such as insulinomas. In addition, as discussed in the review cited, the somatostatin analogue has been studied in patients with GI bleeding (with limited success) and in patients with secretory diarrhea or GI fistulas (better results). The somatostatin analogue is now FDA approved for clinical use in patients with various hormonally active endocrine tumors (marketed as sandostatin).

Tumor Markers

A study by Lappohn and associates describes the use of inhibin measurements as a tumor marker in patients with ovarian granulosa-cell tumors.²⁸ Inhibin is a recently discovered peptide hormone produced by normal ovarian granulosa cells, whose function appears to be to inhibit FSH secretion from the pituitary gland. After inhibin's discovery and characterization in the mid-1980s, a radioimmunoassay was developed for the peptide, allowing extensive study of inhibin's role in normal reproductive physiology. Granulosa-cell tumors may produce inhibin and the plasma level of this hormone may reflect tumor size; it, therefore, may serve as a marker of the primary disease and in the possible detection of tumor recurrences.

Conclusion

I have tried to select recent advances in endocrinology and metabolism that may either have current or future clinical application. Certainly there will be studies not cited which will prove to have significance in clinical endocrinology but hopefully the reader of this review can come away with a greater feel for the types of questions that are currently receiving significant study in endocrinology and metabolism.

References

- Wu MS, Johnston P, Sheulo HH, Hollenbeck CB, Jeng CY, Goldfine ID, Chen YDI, Reavem GM: Effect of Metformin on Carbohydrate and Lipoprotein Metabolism in NIDDM Patients. *Diabetes Care*, 13 (1), 1-8, Jan. 1990.
- Brodsky IG, Robbins DC: Safety of Low-Protein Diets: Where's the beef. *Diabetes Care*, 12 (6), 435-437, June 1989.
- Bougnères PF, Carel JC, Castano L, Boitard C, Gardin JP, Landais P, Hors J, Mihatsch MJ, Paillard M, Chaussain JL, Bach JF: Factors Associated with Early Remission of Type I Diabetes in Children Treated with Cyclosporine. *N Engl J Med*, 318 (11), 663-670, 1988.
- Sauadek CD, Selam JL, Pitt HA, Waxman K, Rubio M, Jeandidier N, Turner D, Fischer RE, Charles MA: A Preliminary Trial of the Programmable Implantable Medication System for Insulin Delivery. *N Engl J Med*, 321 (9), 574-579, 1989.
- Bilous RW, Mavor SM, Sutherland DER, Najarian JC, Goetz FC, Steffes MW: The Effect of Pancreas Transplantation on the Glomerular Structure of Renal Allografts in Patients with Insulin-Dependent Diabetes. *N Engl J Med*, 321 (2), 80-85, 1989.
- Janka HV, Wassam JH, Rand LI, Krolewski AS: Risk Factors for Progression of Background Retinopathy in Long-Standing IDDM. *Diabetes*, 38, 460-464, 1989.
- D'Antonio JA, Ellis D, Doft BH, Becker DJ, Drash AL, Kuller LH, Orchard TJ: Diabetes Complications and Glycemic Control. The Pittsburgh Prospective Insulin-Dependent Diabetes Cohort Study Status Report After 5 yr of IDDM. *Diabetes Care*, 12 (10), 694-700, 1989.
- DCCT Research Group: Diabetes Control and Complications Trial (DCCT) Update. *Diabetes Care*, 13 (4), 427-433, 1990.
- Zavaroni I, Bonora E, Pagliara M, Dall'Aglio E, Luchetti L, Buonanno G, Bonati PA, Bergonzani M, Gnudi L, Passeri M, Reaven G: Risk Factors for Coronary Artery Disease in Healthy Persons with Hyperinsulinemia and Normal Glucose Tolerance. *N Engl J Med*, 320 (11), 702-706, 1989.
- Carr S, Mbanza JC, Thomas T, Keavey P, Taylor R, Alberti KG, Williamson R: Increase in Glomerular Filtration Rate in Patients with Insulin-Dependent Diabetes and Elevated Erythrocyte Sodium-Lithium Countertransport. *N Engl J Med*, 322 (8), 500-505, 1990.
- Position Statement. Standards of Medical Care for Patients with Diabetes Mellitus. *Diabetes Care*, 12(5), 365-368, 1989.
- Palardy J, Havrankova J, Lepage R, Matte R, Belanger R, D'Amour P, Ste-Marie LG: Blood Glucose Measurements During Symptomatic Episodes in Patients with Suspected Postprandial Hypoglycemia. *N Engl J Med*, 321 (21), 1421-1425, 1989.
- Fogelfeld L, Wiviotti MBT, Shore-Freedman E, Blend M, Bekerman C, Pinsky S, Schmeider AB: Recurrence of Thyroid Nodules after Surgical Removal in Patients Irradiated in Childhood for Benign Conditions. *N Engl J Med*, 320 (13), 835-840, 1989.
- Bartalena L, Marocci C, Bogazzi F, Panicucci M, Lepri A, Pinchera A: Use of Corticosteroids to Prevent Progression of Graves' Ophthalmopathy After Radioiodine Therapy for Hyperthyroidism. *N Engl J Med*, 31 (20), 1349-1352, 1989.
- Tezepacz PT, Klein I, Roberts M, Greenhouse J, Levey G: Graves' Disease: An Analysis of Thyroid Hormone Levels and Hyperthyroid Signs and Symptoms. *A J Med*, 87, 558-561, 1989.
- Boucher A, D'Amour P, Hamel L, Fugere P, Gascon-Barre M, Lepage R, Ste-Marie LG: Estrogen Replacement Decreases the Set Point of Parathyroid Hormone Stimulation by Calcium in Normal Postmenopausal Women. *J Clin Endocrinol Metab*, 68 (4), 831-836, 1989.
- Hodsmann HB, Drost DJ: The Response of Vertebral Bone Mineral Density during the Treatment of Osteoporosis with Sodium Fluoride. *J Clin Endocrinol Metab*, 69 (5), 932-938, 1989.
- Pak CYC, Sakhaee K, Zerwekh JE, Parcel C, Peterson R, Johnson K: Safe and Effective Treatment of Osteoporosis with Intermittent Slow Release Sodium Fluoride: Augmentation of Vertebral Bone Mass and Inhibition of Fractures. *J Clin Endocrinol Metab*, 68 (1), 150-159, 1989.
- Riggs BL, Hodgson SF, O'Fallon M, Chao EYS, Wahner HW, Muhs JM, Cedel SL, Melton LJ: Effect of Fluoride Treatment on the Fracture Rate in Postmenopausal Women with Osteoporosis. *N Engl J Med*, 322 (12), 802-809, 1990.
- Storm T, Thamsborg G, Steiniche T, Genant HK, Sorensen OH: Effect of Intermittent Cyclical Etidronate Therapy on Bone Mass and Fracture Rate in Women with Postmenopausal Osteoporosis. *N Engl J Med*, 322 (18), 1265-1271, 1990.
- LaCroix AZ, Weinpahl J, White LR, Wallace RB, Scherr PA, George LK, Cornoni-Huntley T, Ostfeld AM: Thiazine Diuretic Agents and the Incidence of Hip Fracture. *N Engl J Med*, 322 (5), 286-290, 1990.
- Burtis WJ, Brady TG, Orloff JJ, Ersbak JB, Warrell RP, Olson BR, Wu TL, Mitnick ME, Broadus AE, Stewart AF: Immunochemical Characterizations of Circulating Parathyroid Hormone-Related Protein in Patients with Humoral Hypercalcemia of Cancer. *N Engl J Med*, 322 (16) 1106-1112, 1990.
- Budays AA, Nissenson RA, Klein RF, Punk

- K, Clark OH, Diep D, Arnaud CDK, Strewler GJ: Increased Serum Levels of a Parathyroid Hormone-like Protein in Malignancy-Associated Hypercalcemia. *Annals of Internal Medicine*, 111 (22), 807-812, 1989.
- ²⁴ Merenich JA, McDermott MT, Asp AA, Harrison SM, Kidd, GS: Evidence of Endocrine Involvement Early in the Course of Human Immunodeficiency Virus Infection. *J Clin Endocrinol Metab*, 70 (3), 566-571, 1990.
- ²⁵ LoPresti JS, Fried JC, Spencer CA, Nicoloff JT: Unique Alterations of Thyroid Hormone Indices in the Acquired Immunodeficiency Syndrome (AIDS). *Annals of Internal Medicine*, 110 (12), 970-975, 1989.
- ²⁶ Aron DC: Endocrine Complications of the Acquired Immunodeficiency Syndrome. *Arch Intern Med*, 149, 330-333, 1989.
- ²⁷ Gordon P, Comi RJ, Maton PN, Go VLW: Somatostatin and Somatostatin Analogue (SMS 201-995) in Treatment of Hormone-Secreting Tumors of the Pituitary and Gastrointestinal Tract and Non-Neoplastic Diseases of the Gut. *Annals of Internal Medicine*, 110 (1), 35-50, 1989.
- ²⁸ Lappohn RE, Burger HG, Bouma J, Bangah M, Krans M, deBruijn HWA: Inhibin as a Marker for Granulosa-Cell Tumors. *N Engl J Med*, 321- (12), 790-793, 1989.

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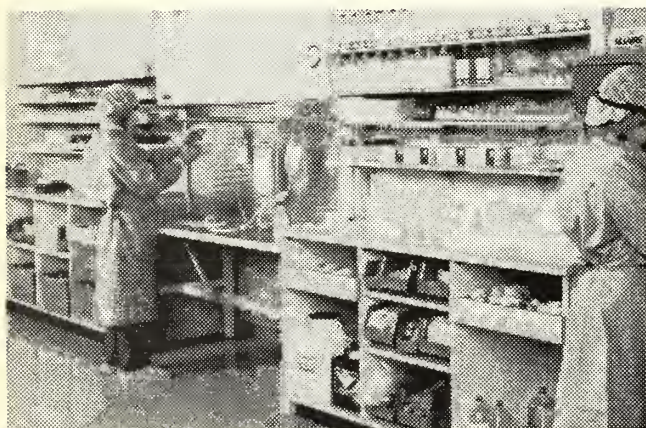
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Psychoneuroimmunology

Byron H. Waksman, MD

Several studies of bereavement have documented diminished immune function associated with hyperfunction of the hypothalamic-pituitary-adrenal axis. . . . Depressed individuals show enhanced morbidity, possibly related to their lowered immune responsiveness.

The research of the last 20 years has made it abundantly clear that there exist multiple interactions among the nervous, endocrine, and immune systems whose full dimensions are yet to be determined. The First International Conference on "Progress in NeuroEndocrinImmunology," held in Italy in October 1988, climaxed a period of rapid growth in the number of published papers and small meetings in this complex field. Its multidisciplinary character can be appreciated by scanning the list of members of the Editorial Board of the journal bearing the same name, which began publication in 1988; distinguished neurologists, psychiatrists, endocrinologists, neuroscientists, and immunologists make up this Board, many

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of them with established credentials in molecular, cell, and developmental biology. A brief survey of the major subjects which define the field, variously known as Neuroimmunology, Psychoneuroimmunology, or Neuro-EndocrinImmunology may be in order at this time.

Neuroimmunologic Diseases

Diseases produced by immune reactions against neural antigens (autoimmune diseases) are well recognized today (Table 1). These may be primarily antibody-mediated or T-cell-mediated, and in many instances, such as myasthenia gravis and the paraneoplastic Eaton-Lambert syndrome, the antigens have been identified and fully characterized. A second group of diseases involves immune responses against infectious agents persistently infecting the nervous system and there is a third group produced by infectious agents acting in the absence of the normal T-cell response (Table 1). In infectious types of neuroimmunologic disease, participation of autoimmune mech-

anisms has been more or less successfully ruled out. Conversely in autoimmune diseases such as multiple sclerosis, the

ABBREVIATIONS USED:

EGF: epidermal growth factor
FGF: fibroblast growth factor
G-CSF: granulocyte colony stimulating factor
GM-CSF: granulocyte-macrophage colony stimulating factor
HPA: hypothalamic-pituitary-adrenal
HPG: hypothalamic-pituitary-gonadal
HPT: hypothalamic-pituitary-thyroid
IL: interleukin
M-CSF: monocyte colony stimulating factor
MHC: major histocompatibility complex
MS: multiple sclerosis
NGF: nerve growth factor
PDGF: platelet-derived growth factor
SP: substance P
TNF: tumor necrosis factor
VIP: vasoactive intestinal peptide

possible involvement of an infectious agent has been often suspected but never proved.

Psychological Elements in Neuroimmunologic Disease

A second group of relationships is found, in the same three groups of diseases, between nervous and immune systems. Psychological trauma or stress has been suspected of playing a role (a) in heightening susceptibility to such diseases as multiple sclerosis, or (b) in precipitating exacerbations of the disease process in those already affected. However, these relationships have not been firmly established by well-controlled observations. They imply an alteration in the level of immune reactivity responsible for producing lesions by stress, ie, by an altered level of function in the hypothalamic-pituitary-adrenal (HPA) axis. On the other hand, the functional level of the hypothalamic-pituitary-gonadal (HPG) axis clearly does play a significant role: women get multiple sclerosis substantially more frequently than men, and the exacerbation rate is strikingly diminished in this same disease during pregnancy.

Immunological disease of the nervous system may entrain major psychologic and psychiatric abnormalities. Two-thirds approximately of multiple sclerosis patients show detectable and sometimes disabling defects of cognitive function (dementia of subcortical type). In addition, many show emotional abnormalities (euphoria, pathological laughing and weeping, depression, bipolar disorder) related to the actual organic lesions, apart from depression consequent upon having a severe, essentially untreatable disease.

In addition, multiple sclerosis is associated with abnormal function of the HPA and HPG axes.

Table 1: Neuroimmunologic Diseases

Immune Reactions Against Neural Antigens (Autoimmune)

Antibody-Mediated

- Myasthenia gravis
- Paraneoplastic syndromes (12 or more)
- Sydenham's chorea
- Stiff man syndrome (and some epilepsy)
- Primary motor neurone disease (a subset of cases)
- Systemic lupus erythematosus affecting the CNS

Cell-Mediated

- Post-rabies vaccination encephalomyelitis and polyneuritis
- Postinfectious encephalomyelitis and polyneuritis
- Multiple sclerosis
- Chronic relapsing inflammatory polyneuropathy
- Adrenoleukodystrophy (inflammation)

Unknown

- Narcolepsy?
- Schizophrenia??

Immune Reactions Against Infectious Agents in Nervous System

Viral

- HTLV-associated myelopathy/tropical spastic paraparesis (HTLV-1)

Bacterial

- Neurosyphilis (*T. pallidum*)
- Tertiary Lyme disease (*B. burgdorferi*)
- Leprosy (*M. Hansenii*)

Infectious Diseases of Nervous System, Determined by Failure of Normal T-Lymphocyte Response

Viral

- Progressive multifocal leukoencephalopathy (JCV)
- Subacute sclerosing panencephalitis (measles, rubella)
- AIDS dementia (HIV-1 and 2)

Other

- Spongiform disorders: Kuru, Creutzfeldt-Jakob disease (prions)

The dexamethasone test, in about half of MS patients, shows the same abnormality as is seen in profound depression. Circulating levels of hypothalamic and pituitary hormones are frequently abnormal. In part, these abnormalities may depend on lesions of MS affecting the hypothalamus directly. On the other hand, the circulating, activated T-lymphocytes characteristic of MS produce ACTH and contribute to this abnormality. Disturbance of sexual function (eg, impotence) has been related in some individuals to disturbed HPG function rather than to lesions (plaques) directly affecting parasympathetic outflow at the sacral level. MS may also be accompanied by major abnormalities of sympathetic nervous function, as shown by disturbed temperature control and

sweating patterns in about half the patients. Beta-adrenergic receptors are markedly increased on the circulating suppressor T-cell population in this disease, but the significance of this alteration remains to be determined.

Molecular Interactions Between Nervous and Immune Systems

Investigation of interactions between the nervous and immune systems in various models with the new tools of molecular and cell biology has uncovered an extraordinary diversity of unanticipated relationships (Table 2). Cytokines produced by the various subsets of T and B-lymphocytes and activated macrophages in actual lesions within the nervous system as well as in the peripheral circulation, have direct effects on the nervous system at

Table 2: Molecules Functioning in Both Nervous and Immune Systems

Cytokines Shown to Have Actions on the Nervous System

Interleukins 1-8
Interferons-alpha/beta, interferon-gamma
Colony-stimulating factors: GM-CSF, G-CSF, M-CSF
Lymphotoxin and tumor necrosis factor
Transforming growth factors alpha and beta

Neural Mediators Shown to Have Actions on the Immune System

Neurotransmitters: Catecholamines, amino acids, GABA
Histamine and serotonin
Neuropeptides: VIP, substance P, somatostatin, opioids

Other Molecules Affecting Both Systems

Growth factors: EGF, FGF, NGF, PDGF
Adhesion molecules and addressins
Arachidonic acid metabolites, PAF

multiple levels. As examples, one might list the actions of interleukin-1 (formerly known as endogenous pyrogen) on the sleep and thermoregulatory nuclei of the hypothalamus, the activating action of interferon-gamma on astrocytes (expression of MHC, production of IL-1, IL-3, and TNF), the destruction of myelin by such TNF, and the interruption of conduction (eg, in AIDS dementia) by cytokines from the virally infected macrophages.

Conversely, specific cells of the immune system are found to respond to the action of traditional neurotransmitters and neuropeptides (Table 2) by enhanced or suppressed function. There is direct beta-adrenergic innervation of all the central and peripheral lymphoid organs and nerve terminals secreting norepinephrine are found in virtually direct contact with lymphocytes at various stages of their development. Similarly there is release of neuropeptides (VIP, SP, and somatostatin) by sensory nerve terminals in lymphoid organs, as well as in or near inflamed sites (eg, in arthritis), where they can directly affect immune cells participating in the inflammatory process. Classical opioid receptors are also found on specific subsets of immunocytes. Even such an unlikely substance as nerve growth

factor has been reported to act directly on B-lymphocytes.

... cytokines, traditionally associated with the immune system, are also produced in the nervous system by neural elements.

A new dimension has been added to this already complex picture by the discovery that cytokines, traditionally associated with the immune system, are also produced in the nervous system by neural elements. Thus IL-1 and TNF are produced by cells of the hypothalamic nuclei and have possible actions as a new class of neurotransmitters. These same molecules and IL-3 are produced by activated astrocytes in inflammatory lesions and produce local tissue damage affecting oligodendrocytes, myelin, and conduction. Finally, and again unexpectedly, traditional neuropeptides (ACTH, TSH, gamma-endorphin) and some of the neurotransmitters are produced by lymphocytes and macrophages. Needless to say, vascular involvement in, eg, the inflammatory lesions of MS is now found to be mediated by both classes of molecules, presumably arising from both sources, in addition to the more traditional effects of im-

mune complexes and the complement cascade. Systemic IL-2, artificially introduced, perturbs the blood-brain barrier and sometimes leads to psychiatric disturbances.

Contemporary studies make use of sensitive immunocytochemical and radioimmunoassay methodologies, as well as *in situ* nucleic acid hybridization and the polymerase chain reaction to identify individual immunologic or neural mediators, their receptors, and the messenger RNAs betokening their synthesis as a means of identifying their exact sites of production and action in nervous system diseases. Observations are made on tissues and body fluids of patients with the diseases under investigation, on well characterized animal models such as experimental autoimmune myasthenia gravis and encephalomyelitis, and on a variety of simpler model systems *in vitro*.

Classical Hormones Interacting with Both Nervous and Immune Systems

The classical endocrine systems exemplified by the HPT, HPA, and HPG axes (Table 3) interact at many levels with both nervous and immune systems. These interactions have been studied with increasing refinement in human and animal models subjected to a variety of manipulations (ablation of organs, injection of hormones), also in relation to circadian and menstrual rhythms, in development and aging, in such states as pregnancy and depression, and finally in congenital abnormalities such as hypopituitary dwarfism.

T-lymphocytes developing in the thymus are regulated by CRF, GnRF, and several of the pituitary peptides, and their sensitivity to adrenal and gonadal steroids is well known. Hypopituitary dwarfism is accompanied by severe

"involutional" abnormalities of the immune system, in particular affecting thymus-dependent cells and responses. Many of the systemic effects of normal aging appear to be mediated by the thymus and by T-cells under HPA,

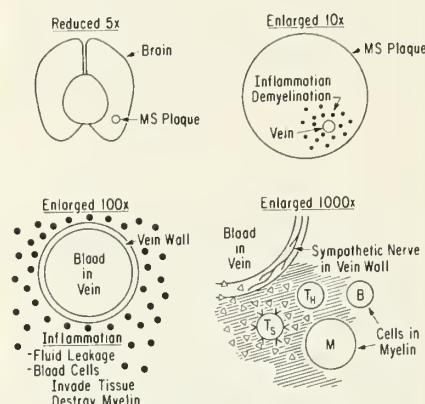
HPT, and HPG regulation. Thus precocious aging in certain mouse strains may be prevented by injections of growth hormone and TSH but not in animals lacking a thymus. As noted earlier, T-lymphocytes make ACTH, TSH,

and certain endorphins, as well as many cytokines and growth factors affecting hematopoiesis.

The repetitive changes in the levels of different hormones during the circadian and menstrual cycles are too well known to need comment. Neurologic and behavioral effects, eg, on sleep and temperature control, and paralleled by changes in steroid-sensitive immunologic functions. There is significant immunosuppression in late pregnancy, in which both steroids and alpha-fetoprotein play a role. The conceptus produces interferon-alpha and oTP-1 (ovine trophoblast protein-1), which are anti-luteolytic and thus promote the pregnancy, also chemotactic factors, which attract lymphocytes and macrophages into the uterine endometrium. The cytokines that these infiltrating cells release stimulate the growth and development of the placenta powerfully. The mother tends to recognize paternal antigens in the fetus and tries to reject it as a foreign graft. This immune response also contrib-

Figure 1:

- Th T helper cell: turns on B and M
 - Ts T suppressor cell: turns off Th, B and M
 - B B cell: makes antibody, helps M attack myelin
 - M Macrophage: attacks and destroys myelin
 - Δ Neurotransmitter molecules (norepinephrine) from sympathetic nerve endings
 - Λ Receptors on Ts: bind and turn on suppressor mechanism; suppress action of other cells
- Fluid leaking from damaged vein; contains antibody, and other substances toxic to myelin



In multiple sclerosis: Release of norepinephrine (Δ) is diminished and receptors (Λ) are increased. There is decreased suppression and therefore increased inflammation and demyelination.

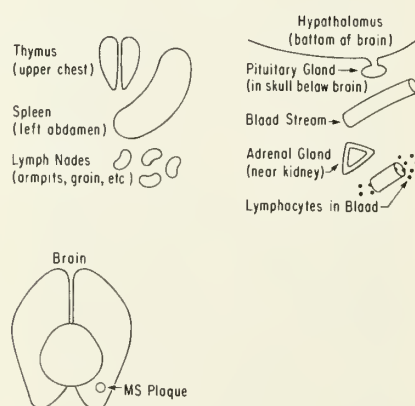
Figure 2:

Lymphoid Organs (where lymphocytes are produced; these make the "immune system").

Sympathetic Nerve Endings in lymphoid organs release norepinephrine which acts on lymphocytes before they enter blood stream and travel to brain.

Neuroendocrine Organs (regulate immune system and other body defenses).

Hypothalamus makes CRF (corticotropin-releasing factor) and acts on pituitary gland; makes ACTH (corticotropin): travels to and acts on adrenal gland; makes norepinephrine and epinephrine, which enter blood: act on lymphocytes travelling between lymphoid organs and "target organ."



In multiple sclerosis: Brain: "target organ"; lymphocytes from blood invade and damage tissue.

Sympathetic nerve endings in vein walls release norepinephrine; normally acts on suppressor cells to hold back inflammation and demyelination.

In multiple sclerosis: Functions of hypothalamic-pituitary-adrenal axis and of sympathetic system are diminished; stress may act through these pathways to change regulation of immune system and increase or decrease formation of new demyelinating lesions in the brain.

Table 3: Classical Hormones Interacting With Both Nervous and Immune Systems

Hypothalamus: CRF (corticotropin releasing factor)
GnRF (gonadotropin releasing factor)
Pituitary: Growth hormone, ACTH (corticotropin)
Thyroid stimulating hormone
FSH, LH, prolactin
Oxytocin, vasopressin
Thyroid: Thyroxine
Adrenal: Corticosteroids
Ovary: Estradiol, progesterone
Testis: Testosterone
Placenta: Chorionic gonadotropin, somatomammotropin
Conceptus: Alpha-fetoprotein

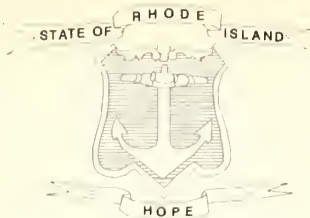
utes to the infiltrative process and local cytokine release in the endometrium.

We have referred to the widely held opinion that psychologic stress can affect immune responses. The extreme example of such stress perhaps is the case of depression. Several studies of bereavement have documented diminished immune function, associated with hyperfunction of the HPA axis, ie, increased secretion of CRF, ACTH, and glucocorticoids and a diminished response to injected dexamethasone. Depressed individuals show enhanced morbidity, possibly related to their lowered immune responsiveness.

Summary

Complex interactions among the nervous, endocrine, and immune systems have been documented and these are currently being studied at the cellular and molecular levels with ever more powerful tools. They have an important impact on diseases affecting the three systems, in particular on autoimmune and infectious diseases of the nervous system. In time neuroimmunological diseases and psychoneuroimmunological relationships may become as "respectable" as the more familiar neuroendocrine diseases and relationships.

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HEALTH BY NUMBERS

Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

A Profile of Rhode Island's Internists, 1990

In conjunction with the relicensure of physicians for 1990, the Board of Medical Licensure and Discipline of the Rhode Island Department of Health initiated collection of selected items of information concerning physicians' medical practices. Included were data on primary and secondary specialty, board certification, and whether or not the physician was in active practice. This information has been aggregated to provide a profile of practicing physicians with reported specialties of internal medicine and its subspecialties.

In response to the 1990 relicensure mailing, a total of 2,307 physicians, including both MDs and DOs, reported being active in practice with mailing addresses in Rhode Island, Massachusetts, and Connecticut. Of the physicians in active practice, 694, or 30.1%, listed primary and/or secondary specialties of internal medicine or its subspecialties. These physicians comprise the largest subgroup of practicing physicians among Rhode Island licensees, with over twice as many physicians as either of the next largest groups, pediatricians and family practitioners.

The pattern of specialties reported by this group is presented in Figure 1. Of the total of 694 physicians, 442 gave internal medicine as their primary specialty, of whom 149 reported an internal medicine subspecialty as their secondary specialty. The latter group has been characterized by the subspecialty in this report. An additional 184 provided an internal medicine subspecialty as their primary specialty. Two smaller groups included those who indicated internal medicine or one of its subspecialties as a secondary specialty with a primary specialty other than internal medicine. Table 1 presents a detailed breakdown of the internal medicine subspecialties reported by internists and subspecialists in the 1990 relicensure response.

The age distribution of internists and subspecialists relative to all practicing physicians shows an increasing number of physicians choosing these specialties during the last two decades (Figure 2).

Table 1: Distribution of Specialties Reported by Internal Medicine Specialists and Subspecialists, Rhode Island, 1990

Specialty	Number	Percent
Internal Medicine, No Subspecialty	338	49
Cardiovascular Diseases	105	15
Gastroenterology	44	6
Pulmonary Diseases	41	6
Hematology	35	5
Endocrinology	29	4
Oncology	24	3
Infectious Diseases	22	3
Geriatrics	18	3
Nephrology	18	3
Rheumatology	18	3
Critical Care medicine	2	<1/2
Total	694	100

Figure 1. Distribution of Internal Medicine Specialists and Subspecialists, by Specialty Category, Rhode Island, 1990

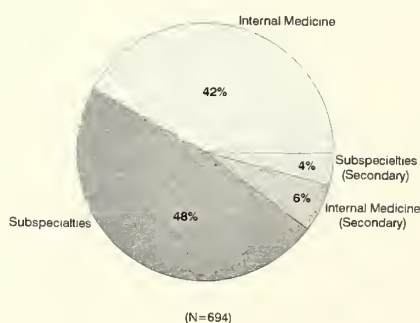


Figure 2. Percentage of Internal Medicine Specialists and Subspecialists among Practicing Physicians, by Age Group, Rhode Island, 1990

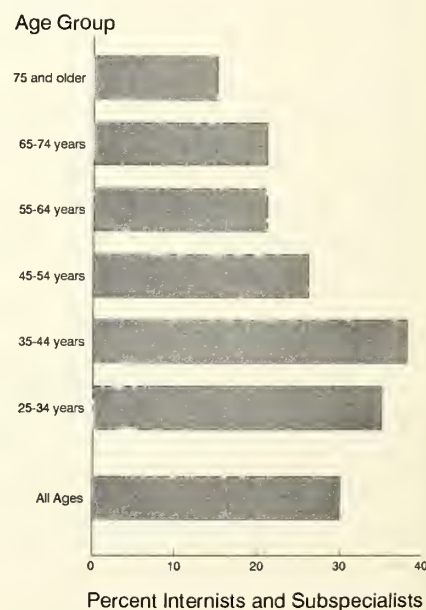


Figure 3. Percentage of Internal Medicine Specialists and Subspecialists Who Are Board Certified, Rhode Island, 1990



The largest proportion of physicians with specialties of internal medicine or its subspecialties occurs among those ages 35-44, followed by those ages 25-34. Among those ages 45 and over, the proportion of internists and subspecialists decreases with age to a minimum level of 15 percent among the most elderly physicians.

The large majority of internists and subspecialists report being board certified in their specialty (Figure 3). Of those specializing in internal medicine and giving no subspecialty, 66% are board certified. Of physicians reporting only an internal medicine subspecialty, 70% report being board certified. Of those reporting internal medicine as their primary specialty and a subspecialty as their secondary specialty, 81% are board certified in internal medicine and 51% are also board certified in their subspecialty.

STATE OF RHODE ISLAND Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoya
State Registrar

Vital Events	Reporting Period	12 Months Ending with July 1990	
	July 1990 Number	Number	Rates
Live Births	1,259	15,654	15.7*
Deaths	815	9,860	9.9*
Infant deaths	(13)	(145)	9.3†
Neonatal deaths	(8)	(114)	7.3†
Marriages	767	8,267	8.3*
Divorces	351	3,856	3.9*
Induced Terminations	599	7,790	497.6†
Spontaneous Fetal Deaths	61	1,167	74.5†
Under 20 weeks' gestation	(57)	(1,067)	68.2†
20+ weeks' gestation	(4)	(92)	5.9†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with April 1990		
	April 1990 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	270	3,389	339.6	4,522.5
Malignant Neoplasms	194	2,424	242.9	6,578.0
Cerebrovascular Diseases	58	603	60.4	770.0
Injuries (Accident, Suicide, Homicide)	36	449	45.0	10,097.0
COPD	41	354	35.5	398.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 998,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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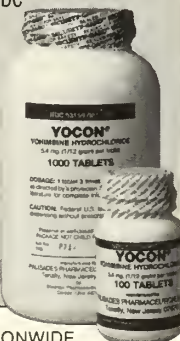
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

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References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Kimberly Allyn
Managing Editor

THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME I
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

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THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (November, 1940)

A single article describing the organization and functions of the newly centralized Rhode Island State Department of Health occupies virtually all of this issue. The Reorganization Act of 1935 had consolidated 17 separate, community-based Boards and Commissions into a single, state-wide Department of Public Health, superceding the authorities of the former entities. The Reorganization Act also transferred the sanitary inspection of shell fish and the inspection and control of milk (about 220,000 quarts per day) from the Department of Agriculture to the Department of Health. The yearly cost (in 1940) to the state is about \$196,000. In addition the new Department receives \$150,000 each year from the Social Security Administration and another \$500,000 to manage the State Sanatorium at Wallum Lake, making an annual budget of close to \$850,000.

As of 1940, the reorganized Department of Health employs 450 people and is divided into the following divisions:

(1) Division of Crippled Children: The object of this division is to locate all children under 21 years with a crippling disorder and

to provide care for those who are judged to be needy. The Division holds weekly diagnostic clinics in various parts of the state. A total of 1,940 children are currently on the Division roster. When a child needs hospitalization, a flat fee of \$4.00 per day is paid which includes all X-ray, laboratory, operating room and hospital bed costs. The Division expends about \$31,000 each year for this purpose, one-half from state appropriations and the remainder from federal and private sources. (2) Division of Maternal and Child Hygiene: Virtually all infants born in rural settings are included in the home visiting program. Practically all children younger than five years, without supervision by a family physician, receive health supervision by state nurses. A well-baby program of weighing and some health supervision is also conducted throughout the state. School and preschool immunization clinics for diphtheria and whooping cough are also available for indigent children. Tuberculin skin testing and pilot dental examination programs are also offered. (3) Division of Preventable Diseases: This division carries four responsibilities: A venereal disease control program and the supervision of treatment clinics in six general hospitals provide free therapy for indigent persons; control measures for

other communicable diseases (particularly tuberculosis); the supervision of the three district health units (Peacedale, Bristol and Woonsocket); and the maintenance of a central statistical registry for cancer. (4) Rhode Island State Sanatorium, Wallum Lake: This facility was established in the township of Burrillville in 1905 for the treatment of tuberculosis. It has a current bed capacity of 574 and the Superintendent is U.E. Zambarano, MD. A new building with 34 additional beds will shortly be opened to provide care for adolescents with tuberculosis. The medical staff consists of the superintendent, 12 resident physicians, one intern and one dentist. During the preceding year, 378 new patients were admitted; artificial pneumothorax was performed 21,393 times; 147 surgical interventions (eg, thoracoplasty, rib resection, etc) were undertaken; 17,239 physiotherapy treatments were given; close to 5,000 X-rays taken; and 2,750 outpatient visits recorded. For paying patients, the inpatient fee is \$10.00 per week, but 79.6% of patients receive free treatment. (5) Division of Life Saving: This unit establishes standards for the training of life guards assigned to the Rhode Island beaches. Since the initiation of this program, the number of drowning deaths has diminished

substantially. (6) Division of Foods and Drugs: This division enforces laws pertaining to adulteration and misbranding of foods and drugs. (7) Division of Examiners: This division contains the boards of examiners for such professions as barbering, dentistry, hairdressing, embalming, medicine, nursing, optometry and pharmacy. Over 15,000 professionals in Rhode Island are legally responsible to this division. (8) Division of Narcotic Drugs and Pharmacies: This unit inspects the 350 pharmacies within the state. (9) Toxicology Laboratory: By chemical, physical or biological laboratory procedures, this unit aids the law-enforcement agencies of the state in detecting crimes and criminals. (10) Division of Sanitary Engineering: This unit is concerned with environmental sanitation regarding water, milk, sewerage, shellfish and industrial plants. (11) Division of Laboratories: The division consists of laboratories in diagnostic bacteriology, serology, pathology, chemistry, food and drug analysis, toxicology.

An editorial requests specialists to volunteer their services, for the newly established Induction Boards, to examine selective service draftees.

Twenty Five Years Ago (November, 1965)

The Public Health Service reported only 35 cases of polio during the first 34 weeks of 1965, a record low.

A notice from Washington states: "A total of 1,529 physicians will be drafted during the first part of next year. The military needs in Viet Nam made necessary an increase in the doctors' draft over the 852 called last January and the 1,000 in January,

1964. The 1966 draft will cover physicians who completed their internships from two to five years ago."

The *Journal* publishes a symposium on the medical and surgical management of peptic ulcer. Jean Todd, MD writes on the etiology of peptic ulcer noting that such lesions occur only near acid-secreting mucosa (ie, duodenum, gastric antrum, esophagogastric junction and Meckel's diverticulum). Factors which increase acid/pepsin secretion include: neurogenic influences, gastrin secretion, histamine, certain genetic factors (eg, blood group O) and various endocrine factors as in the Zollinger-Ellison syndrome. Direct trauma to gastric mucosa, such as with aspirin therapy, must also be considered.

Claude Forkner, MD writes on the medical management of peptic ulcer and stresses the many unanswered questions, such as: What is the cause of chronic, recurrent peptic ulcer? Why are blood group O persons more susceptible to peptic ulceration? Why is peptic ulcer ten times more common in males? Why does the stomach not digest itself? What is the role of salivary secretion in peptic ulcer? What is the role of Brunner gland secretion? Is there an inhibitory pyloric gland hormone? The author then outlines his principles of treatment of uncomplicated, idiopathic peptic ulcer: Therapy should correct or neutralize emotional problems, excess acid secretions, irritating foods, irritating fluids (eg, alcohol), and gastroduodenal spasms.

Samuel W. Moore, MD describes the surgical management of peptic ulcer, particularly the complications of perforation, bleeding and enteric obstruction.

Herbert Fanger, MD and colleagues summarize their work in the Rhode Island Women's Can-

cer Cytology Survey and describe the results of 77,650 cytologic examinations. Uterine or cervical cancer, verified by tissue analysis, was detected in 298 cases.

Jay Orson, MD and J. Brian May, MD describe lead intoxication in 19 Rhode Island children, all diagnosed during a period of two years. Most of these children presented a history of pica and a variety of gastrointestinal and nervous system symptoms. All were between the ages of one and one-half and four years; over half of the affected children were Black. Two died and "an unknown number of the remainder will evidence some degree of permanent brain damage."

E.F. Hall, MD presents a paper on the responsibilities of local, state and federal agencies in controlling institutionally required infections.

A *Journal* editorial notes that an annual lectureship is established to honor Alex M. Burgess, MD. The editorial also lists ongoing lectureships and visiting appointments honoring the contributions of prominent Rhode Island physicians including: Isaac Gerber, Nathan Kiven, Murray S. Danforth, Arthur H. Ruggles, John F. Kenney, Maurice Kay, and J. Murray Beardsley.

Rhode Island Medical Society



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Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

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Volume 73, Number 12



Public Health in Rhode Island

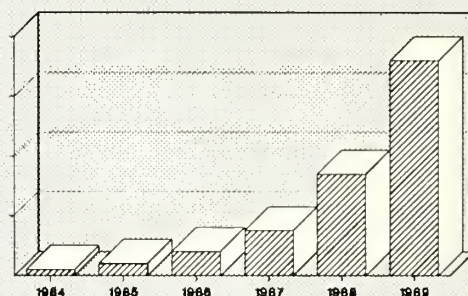


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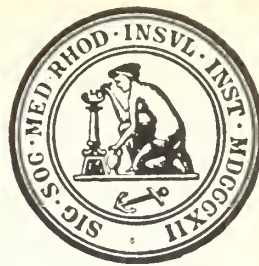
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Cancer Control: The Role of the Physician

It has been a privilege to work with the members of the Department of Health's Cancer Control Committee in the development of the *Rhode Island Cancer Control Plan 1990-1992*¹ (See related article page 583). I was impressed by the strides that our state is making in preventing, detecting and treating malignant disease. Nonetheless, there is always room for improvement.

Meeting the Cancer Control Plan's aggressive goal of reducing cancer mortality by 33%, ie, eliminating 800 to 1000 cancer deaths annually, by the year 2000, will take major commitment by individual Rhode Islanders, community leaders and health professionals. In particular, physicians will play a central role in achieving this goal, by:

Prevention: Counseling patients to stop smoking.

The National Institute of Health's *Review and Evaluation of Smoking Cessation Methods: The United States and Canada, 1978-1985* states: "Most smokers state that they are aware of the health risks of smoking; (and) they view the physician as an important person in their decision to quit smoking."² This same report estimates that, if physicians counseled all of their patients who smoke on how to stop and were successful with just 4% of patients, the yield would be 1.5 million ex-smokers nationally. In Rhode Island, this success rate would yield over 7000 ex-smokers, a major contribution to the objectives of the Rhode Island Cancer Control Plan.

Screening: Recommending and performing breast, cervical and oral cancer screening exams.

In the landmark Health Insurance Plan of New York study, conducted in the mid 1960s, it was found that at least 19% of the breast cancer deaths among women in the United States could be attributed to the nonuse of mammography.³ Subsequent research has found that the proportion of deaths that could be prevented through appropriate use of mammography may be as much as one-third. A recent article in *Morbidity and Mortality Weekly Report*, "Trends in Breast Cancer Screening — Rhode Island, 1987-1989" found that the percentage of Rhode Island women who had received screening mammography in the past year had increased from 31% to 40% in just 15 months.⁴ The editorial note accompanying this article states: "Physicians' recommendations may account for much of the increase in screening rates. . . . In Rhode Island, adherence to screening guidelines by women and physicians is improving. These trends must continue if breast cancer screening is to become common practice among women at risk."⁴ Rhode Island is already recognized as a leader in breast cancer screening, but much remains to be done: In 1989 a majority of eligible women were not being screened according to current guidelines.

Many deaths from cervical cancer and oral cancer are avoidable. The fact that many of these tumors are not detected in early, treatable stages is tragic. How-

ever, effective screening techniques are readily available for these cancers, and if they are a routine part of patient examinations, there will be further decreases in unnecessary mortality from these cancers.

Treatment: Encouraging and participating in multidisciplinary management of cancer treatment.

The National Cancer Institute has estimated that our nation's overall cancer death rate could be reduced by at least 10% by the year 2000 through universal application of state-of-the-art therapy.⁵ The key to achieving this goal is *multidisciplinary management* of cancer patients. The complex advances in cancer treatment achieved in the past two decades require the perspective of surgeons, medical oncologists, radiation therapists, pathologists, and physicians skilled in diagnostic imaging. No one specialist can be well versed in all aspects of treatment. Effective collaboration among the disciplines is necessary to bring the current "best" treatment to the patient. Effective collaboration, however, is no easy task, especially as a larger percentage of cancer patients are treated in ambulatory settings. Working together will take commitment and creativity. But the stakes are high — 250 lives a year in Rhode Island, alone.

As Director of Health, I am committed to the goals and objectives so thoughtfully developed by the members of the Cancer Control Committee, and I urge all physicians in Rhode Island to

work in their practices and with their colleagues to meet the Committee's challenge: Eliminate one-third of all cancer deaths in our state by the year 2000.

H. Denman Scott, MD
Director, Rhode Island
Department of Health

References

- ¹ Rhode Island Department of Health, "Rhode Island Cancer Control Plan for 1990-1992." December 1990.
- ² Schwartz, JL, "Review and Evaluation of Smoking Cessation Methods: The United States and Canada, 1978-1985," Published by the National Cancer Institute, NIH Publication No. 87-2940, April 1987.
- ³ Centers for Disease Control, "Chronic Disease Reports: Deaths from Breast Cancer among Women — United States 1986." *MMWR*, 1989;38:565-569.
- ⁴ Buechner, JS; Fulton, JP; Feldman, JP; DeBuono, BA and Kovenock, D, "Trends in Breast Cancer Screening — Rhode Island, 1987-1989." *MMWR*, 1989;38:569-571.
- ⁵ National Cancer Institute, "Cancer Control Objectives for the Nation: 1985-2000," *NCI Monographs*: 1986 No. 2.

The Rhode Island Department of Health

Fifty-five years ago in Rhode Island, legislation was enacted which led to the consolidation of the seventeen separate, community-based Health Boards and Commissions into a single, state-wide Department of Health. In 1940, the newly centralized Department employed 450 people assigned to eleven divisions variously concerned with: (1) crippled children; (2) maternal and child hygiene; (3) preventable diseases (primarily tuberculosis and syphilis); (4) Wallum Lake Sanatorium (now called Zambardo Hospital); (5) life saving; (6) foods and drugs; (7) boards of examiners; (8) narcotic drugs and pharmacies; (9) toxicology; (10) sanitary engineering; and, (11) laboratories.

In the half century since its centralization, the Department has exerted an increasingly important

role in improving the health of this community. The Department's mission, 50 years ago, was to insure the sanitary state of Rhode Island's water, milk and food supply; to provide some clinic facilities for crippled children and impoverished mothers and children; to administer a variety of state functions such as licensure boards; and to offer some modest aid in toxicologic and other laboratory aid, when in behalf of the public health.

Our current Department of Health, deemed one of the best and most efficient in the nation, has expanded its responsibilities materially. Its current purpose is:

The primary mission of the Rhode Island Department of Health is to protect and promote the health of the population and to prevent disease through life-style change, environmental protection, and health care delivery. The Department employs educational, regulatory, financial and programmatic initiatives in the pursuit of health promotion/disease prevention. The science of epidemiology is the common thread which links and guides all of the Department's endeavors.

With approximately the same number of personnel as in 1940, the Department now exercises a broader mandate and engages in actions which promote the health of a greater percent of our population. Many of its present activities are prospective, often educational in character, thus leading to the prevention of disease, disability and death.

Newer departmental functions include comprehensive computer-driven systems of vital statistics; surveillance of environmental, occupational and radiologic factors in the community; health planning; health promotion; cancer registry; emer-

gency medical services; drug control; nutrition; dental health; disease control, including chronic disease such as diabetes, and newer sexually transmitted diseases such as AIDS.

In addition to its customary tasks, the Department has identified the following additional problems to address in the next two years:

- Make certain that the 14,000 Rhode Island women and children continue to receive nutrition counselling and supplemental foods.
- Assess the medical risks related to environmental health hazards and occupational exposures including chemically-induced organ toxicity, cancer and adverse pregnancy outcomes. Review environmental health standards for contaminants in air, water and food.
- Evaluate disease clusters in Rhode Island.
- Regulate more properly the nearly 500 public drinking water systems in the state.
- Study more carefully the wide variety of significant occupational health problems particularly in the employees of small companies.
- Provide better information on the etiology and epidemiology of human cancers.
- Study the residential, medical and social needs of the approximately 36,000 dependent elderly in the community.
- Develop more information concerning the abuse of licit and illicit drugs in the community.
- Maintain the Board of Medical Licensure and Discipline which currently investigates and adjudicates about 150 public complaints per year as well as about 75 settled malpractice claims each year. (In the state there are approximately 2,800

licensed physicians and 500 house staff with limited licenses).

- Approximately 200,000 Rhode Islanders are injured each year, severely enough to require medical attention or restricted activities for at least one day. Emergency facilities (emergency rooms, ambulances, etc.) must have uniformly high standards in training, equipment, data systems and communications.
- There remains a significant gap between white and non-white mortality rates in Rhode Island.
- Many pregnant women do not have appropriate health insurance.
- Fifty years ago, many diseases were related to a nutrient deficiency. Today these deficiency diseases have been virtually eliminated but are replaced by diseases of nutrient excess or imbalance.
- There are about 275 reported cases of AIDS in the state and an estimated 3 to 4,000 residents infected with the HIV virus.
- There are 35,000 diabetics in Rhode Island.
- During 1990, about 650 Rhode Island women will develop breast cancer and 250 will die from the disease.

This list represents some of the challenges which are better addressed when the public health sector and the individual practitioners work jointly and collectively toward identified objectives. This issue of the *Journal* directs our attention to a few of these Department of Health programs.

Stanley M. Aronson, MD

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Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

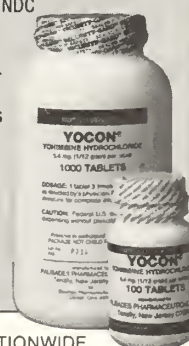
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon[®] 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Rhode Island's Contributions to Medicine

Rhode Islanders, living in the smallest of the states and the last of the original thirteen to ratify the Constitution, often bring modesty regarding their state to a high art form. When asked for their address, Rhode Islanders frequently provide it with apology, sometimes responding with "Little

Rhody" as a means of deflecting an anticipated sarcasm. The more assertive ones, when asked whether they have lived all their lives in Rhode Island, respond, not yet!"

Yet, in the fields of medicine, medical education and public health, Rhode Islanders have

done more than their share in providing national leadership. And in recognition of this great heritage, the *Rhode Island Medical Journal* will publish, from time to time, brief biographical summaries of these leaders born or raised in the Ocean State.

The Father to New England Medical Schools

Nathan Smith, the son of a surveyor father and a midwife mother, was born on September 30, 1762. The Smith family had left Norfolk, England in 1638 for religious reasons and established their home on the banks of the Seekonk river in the Newman Settlement, then a part of Rehoboth, Massachusetts. (In 1862, the western part of Rehoboth had been ceded to Rhode Island and is now a part of East Providence). The family later moved to Vermont and Smith served in the Vermont militia during the Revolutionary War.

Smith began his civilian career as a local school teacher, although there is no record that he had ever received formal schooling. A few years later, happenstance led him to assist a traveling surgeon in performing an amputation. To this surgeon, Dr Josiah Goodhue, he expressed an interest in the profession of medicine and was told that further education was needed before he might be accepted for a medical apprenticeship. Smith then devoted the next year to intensive preparation and began his profes-

sional apprenticeship in 1784. Three years later, without benefit of any diploma, he began practice in Cornish, New Hampshire.

The daily frustrations of rural practice convinced him of his grave educational inadequacies and he then registered at Harvard, attending classes conducted by Drs John Warren, Benjamin Waterhouse and Aaron Dexter. During his student-days, Smith lodged in Waterhouse's home. In 1790, at age 28, Smith was awarded the MB degree, the only medical degree recipient for that year. He then resumed his practice in New Hampshire.

Despite a successful practice, Smith grew increasingly restive with the paucity of educational facilities in the new nation. At this time there were but three medical schools in the United States at the Universities of Pennsylvania, Columbia and Harvard. Smith had once even proposed a county lottery, the proceeds to be invested in a central medical library.

In the belief that medical education would best flourish within a university, Smith in 1796 applied to Dartmouth College for a

professorship in the theory and practice of medicine. His novel proposal for a school of medicine was approved the following year and in the interim Smith sailed for England, attending lectures in Edinburgh and London, while also purchasing texts and laboratory instruments to enrich his contemplated medical school. Formal teaching began in the autumn of 1797 in a single room which served as office, classroom, library, laboratory and dissection chamber, with Smith as the sole faculty. His income was derived exclusively from lecture fees and the private practice of medicine.

The success of Dartmouth's medical school led to requests for further investment in scientific apparatus and in 1803 the New Hampshire legislature appropriated \$600 for this purpose. By 1810, the flourishing school now operated in an elegant brick building paid for partially by the state and partially through generous gifts from Smith. Tuition for the 77 registered medical students was \$133 for two terms.

In 1812 Yale elected to establish a medical school and invited

Smith to be its organizer and first professor of medicine (despite the initial opposition of Yale's President, Timothy Dwight, who believed that Smith had been unduly influenced by the writings of the liberal Thomas Paine). From its beginnings in 1813, the Yale medical school was a highly successful enterprise. (Smith was father to four sons and six grandsons all of whom later graduated from Yale's medical school. Smith also had five daughters but their activities are obscured in the shadows of history).

In 1820, the Maine legislature established and endowed a medical school at Bowdoin College, the alma mater of Longfellow and Hawthorne. Smith was its first professor and classes were begun in 1821 with 21 registered students. Smith continued at Yale but now engaged in a seasonal pattern of shuttle-teaching between Maine and Connecticut.

Following his belief that each New England state should have "... one medical school and no more," Smith founded yet another school of medicine in Burlington, Vermont, in the year 1825. He was aided in this effort by his son, Dr Nathan Ryno Smith, a recent graduate of Yale medical school. Smith's itinerant teaching now extended to three campuses prompting Dr Oliver Wendell Holmes, years later, to remark, "He occupied not a chair but a whole Settee!" Dr Nathan R. Smith, the son, apparently inherited his father's zeal for starting medical schools and went on to cofound three further, including Jefferson Medical School in Philadelphia.

By 1826 Smith had fulfilled his objective of establishing medical schools in each New England state (Massachusetts and Rhode Island already had medical schools at Harvard and Brown).

The Medical Schools of New England 1776-1827

Harvard (Massachusetts)	1782
Dartmouth (New Hampshire)*	1797
Brown (Rhode Island)	1811†
Yale (Connecticut)*	1812
Castleton (Vermont)	1818‡
Bowdoin (Maine)*	1820‡
Vermont (Vermont)*	1825
Berkshire (Massachusetts)	1825‡
Woodstock (Vermont)	1827‡

*: founded by Nathan Smith

†: closed in 1827; reestablished in 1972.

‡: no longer in existence

Smith was taken gravely ill, likely influenza, in the winter of 1828; shortly thereafter he developed signs of cerebral infarction and passed away on January 26, 1829 at age 67.

His contributions went beyond

the realm of medical education: Smith was regarded as an outstanding surgeon; he worked with state legislatures to establish the licensing of anatomy classes and he was a leader in the identification and suppression of quackery; he was also the President of the New Hampshire Medical Society and his seminal scientific writings illuminated such disparate subjects as typhoid fever, blood circulation and newer orthopedic procedures. Yet his role as a teacher and the founder of four of New England's medical schools is the accomplishment for which he is best remembered. Henry Adams — another great New Englander — once said, "A teacher affects eternity. He can never tell where his influence stops."

Stanley M. Aronson, MD

HAPPY HOLIDAYS TO YOU AND YOURS

from the

EDITORIAL STAFF

RHODE ISLAND MEDICAL JOURNAL



Dr. Holwick outside of hospital where she practices as a civilian traumatologist



Dr. Holwick in operating room at Letterman Army Medical Center.

JANN L. HOLWICK, M.D.

General and Trauma Surgeon.
Captain, U.S. Army Reserve.

EDUCATION University of Southern California, B.S.;
University of California School of Medicine.

RESIDENCY Harbor General Hospital—UCLA
Medical Center.

HOSPITAL AFFILIATIONS St. Luke Hospital;
Huntington Memorial Hospital, Pasadena, California;
Traumatologist, Arcadia Methodist Hospital, Arcadia,
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- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:

- Hypersensitivity reactions have been reported in about 1.5% of patients and include morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions have been reported with the use of Ceclor. These are characterized by findings of erythema multiforme, rashes, and other skin manifestations accompanied by arthritis/arthralgia, with or without fever, and differ from classic serum sickness in that there is infrequently associated lymphadenopathy and proteinuria, no circulating immune complexes, and no evidence to date of sequelae of the reaction. While further investigation is ongoing, serum-sickness-like reactions appear to be due to hypersensitivity and more often occur during or following a second (or subsequent) course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults with an overall occurrence ranging from 1 in 200 (0.5%) in one focused trial to 2 in 8,346 (0.024%) in overall clinical trials (with an incidence in children in clinical trials of 0.055%) to 1 in 38,000 (0.003%) in spontaneous event reports. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy; occasionally these reactions have resulted in hospitalization, usually of short duration (median hospitalization = two to three days, based on postmarketing surveillance studies). In those requiring hospitalization, the symptoms have ranged from mild to severe at the time of admission with more of the severe reactions occurring in children. Antihistamines and glucocorticoids appear to enhance resolution of the signs and symptoms. No serious sequelae have been reported.
- Stevens-Johnson syndrome, toxic epidermal necrolysis,

and anaphylaxis have been reported rarely. Anaphylaxis may be more common in patients with a history of penicillin allergy.

- Gastrointestinal (mostly diarrhea): 2.5%
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1% and, rarely, thrombocytopenia and reversible interstitial nephritis.

Abnormalities in laboratory results of uncertain etiology.

- Slight elevations in hepatic enzymes.
- Transient lymphocytosis, leukopenia, and, rarely, hemolytic anemia and reversible neutropenia.
- Rare reports of increased prothrombin time with or without clinical bleeding in patients receiving Ceclor and Coumadin concomitantly.
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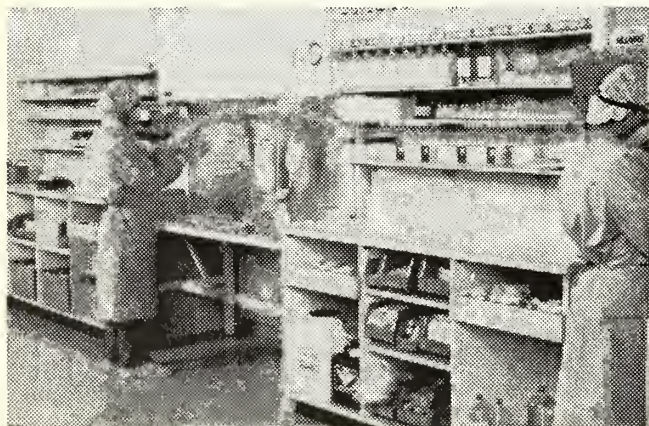
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Cancer Control in Rhode Island: Blueprint for the 1990s

H. Denman Scott, MD
John P. Fulton, PhD
Melinda Komiske, MS

Cancer mortality is approximately 10% higher in Rhode Island than in the US . . .

Cancer in Rhode Island: Reality and Potential

Rhode Island has one of the highest cancer mortality rates in the nation. Cancer mortality is approximately 10% higher in Rhode Island than in the US as a whole, even when differences in age, gender, and race have been controlled. About 5000 new cases of cancer are diagnosed annually among Rhode Islanders, and between 2000 and 2500 Rhode Island residents die of the disease.

H. Denman Scott, MD, is Director of the Rhode Island Department of Health and Clinical Professor of Medicine at Brown University, Providence, Rhode Island.

John P. Fulton, PhD, is Administrator of the Rhode Island Cancer Registry, Rhode Island Department of Health, and Clinical Assistant Professor of Community Health at Brown University, Providence, Rhode Island.

Melinda Komiske, MS, is Chief of the Office of Health Planning at the Rhode Island Department of Health, Providence, Rhode Island.

Cancer accounts for about one of every four deaths in Rhode Island.¹

As in other urban areas, Rhode Island's high cancer mortality rate is caused by a few cancers, most notably cancer of the lung, colon-rectum, and breast. Deaths from these three cancers account for almost 50% of all cancer deaths in the state. Mortality from most other cancers is about the same in Rhode Island as elsewhere in the US. Rhode Island's urban cancer profile is attributable in the main to lifestyle factors such as smoking, alcohol consumption, and possibly the consumption of fatty foods. Occupational exposures may also elevate death rates.²

Much can be done to reduce cancer mortality in Rhode Island. Changes in lifestyle and the proper use of screening tests would prevent up to 725 deaths a year from cancers of the lung, colon-rectum, and breast, alone. By not smoking, Rhode Islanders would prevent 87% of lung cancer deaths. By limiting fat in the diet and increasing the consumption of dietary fiber, it is estimated that Rhode Islanders might prevent 50% of deaths from colorectal cancer. If all women ages 40 and over were screened for breast

cancer according to current guidelines, between a fifth and a third of all deaths from breast cancer would be avoided. Other cancers would also yield to prevention and screening, and many lives would be saved annually if more Rhode Islanders received state-of-the-art treatment for a wide variety of cancers.^{3,4}

The State's Approach to Cancer Control

In 1985 the Rhode Island state legislature passed "An Act Related to Cancer," which was signed by the Governor and became law. The Act charged the Director of Health with conducting "such activities to prevent and control cancer among the residents of the state as he shall deem necessary and appropriate," and officially created the Rhode Island Cancer Registry, funding

ABBREVIATIONS USED:

AJCC: American Joint Cancer Committee
CDC: Centers for Disease Control
CEA: carcino-embryonic antigen
ER: estrogen receptor
NCI: National Cancer Institute
PR: progesterone receptor

cancer control activities with revenues from the sale of cigarettes.

In July 1986 the Rhode Island Department of Health (the Department) established the Rhode Island Cancer Registry, hiring staff and signing a contract with the Hospital Association of Rhode Island for data collection, cleaning, and quality assurance activities. This collaboration has grown into a strong working relationship between the two organizations.

Changes in lifestyle and the proper use of screening tests would prevent up to 725 deaths a year (in Rhode Island) from cancers of the lung, colon-rectum and breast, alone.

About the same time, the Department began the development of a statewide breast cancer screening program, using funds from the state appropriation for cancer control activities. The program, which officially opened in November, 1987, offered low-cost screening mammograms to women ages 40 and over. Most radiology units in the state participated, using dedicated mammography units. Comprehensive quality assurance procedures were built into the program, supported in part by several grants from the Centers for Disease Control (CDC) in Atlanta. Breast cancer screening was promoted among primary care physicians with a direct mailing and selected talks, and among eligible women with a year-long multi-media campaign. The state legislature assisted by passing "An Act Relating to Health Insurance — Coverage for Mammograms and Pap Smears," which mandated universal insurance coverage for screening mammograms and Pap tests, beginning in September, 1988. In the first year and a half

of the breast cancer screening program, the proportion of eligible Rhode Island women screened according to current guidelines increased from 30% to 41%. Also, the success of the program's initial quality assurance activities led to the funding of similar activities for cervical cancer screening, including surveillance, the formation of a statewide cervical cancer quality assurance advisory committee, and the drafting of standards for cervical cancer screening.

In mid-1986, the Rhode Island state legislature passed "An Act Relating to Health Education, Alcohol and Substance Abuse Prevention," to support universal school health education in grades K-12. This law has become the foundation for smoking prevention efforts in the state. Like the Cancer Registry, universal school health education is supported with revenues from the sale of cigarettes. It contains anti-smoking subject matter in all grades and is evaluated annually by testing in the schools. The Department of Health has built on this foundation, competing for anti-smoking funds from the National Cancer Institute (NCI). Most recently, the Department, the Rhode Island Division of the American Cancer Society, and other Rhode Island organizations are submitting a proposal for Project ASSIST, the nation's main anti-smoking initiative for the 1990s, funded jointly by the NCI and the American Cancer Society.

In December 1987 the Department convened a Cancer Control Committee to plan priority cancer control activities for the 1990s. The Director of Health invited 24 health care professionals to serve on the Committee, including physicians, nurses, a dentist, and health care administrators. The Committee reviewed comprehensive statewide cancer statistics

and estimates prepared by the Department's Office of Health Statistics, then divided into four subcommittees: cancer prevention, cancer screening, oral cancer screening, and cancer treatment. Each subcommittee expanded by recruiting additional members from the community who had special expertise in these fields. In all, 46 people served (Table 1). Each subcommittee drafted a report on the cancer control needs of the state. These reports were reviewed by the Cancer Control Committee as a whole, critiqued, then excerpted to form the basis of a statewide Cancer Control Plan for the years 1990-1992. The Plan focuses on cancers of the lung, colon-rectum, breast, cervix, and oral cavity. By the fall of 1989, the Plan had been sufficiently polished by the Committee to undergo public scrutiny, and comments were received in public hearing. The Committee reconvened to discuss suggested revisions from the public at large, made modifications to the plan, then presented it to the Director of Health, who accepted it in December, 1989. The plan was printed, formally announced by the Governor, and distributed widely among Rhode Island's health professionals in the spring of 1990. The Cancer Control Committee will reconvene to review and revise the Plan in 1992, and periodically to address urgent cancer control issues as they arise.⁵

Rhode Island's Cancer Control Plan, 1990-1992

The Cancer Control Plan (the Plan) specifies objectives for prevention, screening and treatment, using a format developed by the national Model Standards Project.⁶ Objectives contain target dates and outcomes. Many of the

Table 1. Committee Members and Staff

Members

David Abrams, PhD
Miriam Hosp.
A

Jeffrey Bastable
Westerly Hosp.
D, M

Peter Baute, MD
Kent County Mem. Hosp.
A, D, M

Richard Bender, DDS
Veterans Adm. Med. Ctr.
C

Roger Brotman, MD
Radiation Onc. Assoc.
D, M

Paul Calabresi, MD
Roger Wms. Gen. Hosp.
D, M

David Chatel
Amer Heart Assoc.
A

Mary P. Colbert, MD
Rhode Island Hosp.
B, M

Francis J. Cummings, MD
Roger Wms. Gen. Hosp.
D, M

Dolores DiOrio
RI Dept. of Health
D

Ruth Eshleman, PhD
URI Food Service
A

Judith Feldman, MD
RI Dept. of Health
D

Arvin Glicksman, MD
Roger Wms. Gen. Hosp.
A, D, M

Richard R. Gordon, DMD
Johnston, RI
C

David Greer, MD
Brown University
B, M

Arnold Herman, MD
Providence, RI
D

Laura Hilderley, RN, MS
Maddock Radiation Onc.
D, M

Delanson Hopkins
Rhode Island Hosp.
M

Jacqueline Janicki, RN, MS
Island Hospice-Newport
A, D, M

Margaret Kane
RI Lung Association
A

Jila Khorsand, MD
RI Soc. of Pathology
M

Robert Knisley, MD
Brown University
D, M

Thomas M. Lasater
The Memorial Hosp.
A

Louis Leone, MD
Rhode Island Hosp.
A, D, M

Jane E. Ligums, DMD
RI Hosp. Dental Ctr.
C

Robert Marshall, PhD
RI Dept. of Health
C

Bela Matyas, MD, PhD
RI Dept. of Health
A

Eric Mazur
Miriam Hosp.
D, M

Patricia Mitchell, MSN
Rhode Island Hosp.
D, M

Alan Morrison, MD, PhD
Brown University
B, M

John Parrillo, DMD
RI Dept. of Health
C

Vishram B. Rege, MD
Rhode Island Hosp.
C

David Rehm
Hospice Care of RI
D, M

Albert Schilling, MD
Rhode Island Hosp.
A

H. Denman Scott, MD, MPH
RI Dept. of Health
M

Charles Shoemaker, MD
Newport, RI
D, M

Robert Sholler, DMD
RI Dental Assoc.
C

Steven E. Slaughter
Amer. Cancer Soc.
B, M

Mohsen Soltani, MD
St. Joseph's Hosp.
B, M

Dorothy Stanis
Hospital Assoc. of RI
D, M

David Stoll, MD
Landmark Hosp.
C, D, M

John Turner, II, MD
Providence, RI
B, M

Alan Ventetuolo
Amer. Cancer Soc.
A

Joseph Yacavone, DMD, MPH
RI Dept of Health
C

Staff

Melinda Komiske, MS
RI Dept. of Health
A, D, M

John P. Fulton, PhD
RI Dept of Health
B, C, M

A = Prevention Subcommittee
B = Screening Subcommittee
C = Oral Cancer Subcommittee
D = Treatment Subcommittee
M = Cancer Control Committee

outcomes are quantified. For example, the first prevention objective states: "By 2000, the proportion of persons 19 years of age and over who smoke should decrease from 24.3% to less than 15%." The Plan also suggests actions to achieve outcomes, and contains specific recommendations for screening and treatment.

Prevention

Prevention objectives, which have been designed to cut cancer mortality 16% between 1990 and 2000, focus squarely on smoking prevention and cessation. An estimated 30% of all cancers are caused by tobacco use, including an estimated 87% of all lung cancers.¹ In Rhode Island, lung cancer alone accounts for 25% of all cancer deaths.¹ The Plan calls for cutting the proportion of smokers by the year 2000 as follows:

- Among adults, from 24.3% to less than 15%;
- Among teens in grades seven through twelve, from 24% to 6% or less;
- Among pregnant women, to 7.5% or less;
- Among minority and low income groups, to 15% or less.

Prevention objectives also call for increased restrictions on smoking in public places:

- By 1995, reduce or eliminate exposure to environmental tobacco smoke in the work place, schools and public places.

Three additional prevention objectives aim to build the state's ability to monitor dietary, environmental, and occupational risks:

- By 1990, establish a data collection system to monitor the dietary patterns of Rhode Islanders, focussing on the consumption of calories, fat, fiber, and alcohol.
- By 1990, establish surveillance systems to monitor radon exposure and sun exposure in

Rhode Island; continue monitoring air quality. (The Department is considering surveillance of the use of sun block agents as an alternative to the surveillance of sun exposure).

- By 1995, establish a system to monitor the cancers most strongly related to occupational exposures, including cancers of the lung, liver, pancreas, kidney, bladder, brain, leukemias and lymphomas.

Screening

Cancers of the breast, cervix and oral cavity have been targeted for screening. Breast cancer causes 200 deaths a year in Rhode Island.¹ Between one-fifth and one-third of those deaths would be avoidable if all eligible women were screened according to current guidelines.^{3, 4} Cancer of the cervix claims about 15 deaths a year.¹ Although this number is small, virtually all deaths from cervical cancer are considered avoidable.⁷ Cancers of the oral cavity account for about 40 deaths a year among Rhode Island residents.¹ Most are caused by tobacco use, and would be prevented if tobacco use were eliminated.⁴ Many may be detected in early stages of growth. Early detection and treatment increases the probability that primary tumors may be reduced or removed without gross disfigurement of the head and neck, thus enhancing quality of life, and increases the probability of survival, as well. The effectiveness of breast and cervical cancer screening in reducing mortality has been demonstrated in the scientific literature.³ Although the effectiveness of oral cancer screening has not been tested in large population-based trials, it is widely accepted that early detection of oral cancer facilitates treatment and saves lives. The major screening objectives include:

- By 2000, the proportion of women 40 years of age and over who are screened for breast cancer according to the recommendations of the Rhode Island Cancer Control Committee (Table 2) should increase to 80%.
- By 2000, the proportion of women 20 years of age and over who are screened for cervical cancer according to the recommendations of the Rhode Island Cancer Control Committee (Table 2) should increase to 95%.
- By 1991, 50% of oral examinations should include a complete tissue screening examination (Table 2) for oral cancer. By 1995, 95% of oral examinations should include a complete tissue screening examination for oral cancer.

Large population-based trials of colo-rectal screening are currently underway, but have not yet demonstrated reductions in mortality among those people who have been screened according to study protocols.³ Accordingly, the Plan also directs public health officials to "monitor the scientific literature on colo-rectal screening," planning for efficient and safe colo-rectal screening in Rhode Island if its effectiveness is demonstrated in screening trials.

Treatment

Among a wide variety of potential treatment objectives, the Cancer Control Committee chose to focus on the treatment of breast cancer in its first edition of the Plan. At the time, breast cancer accounted for more deaths among women than all other cancers, about 200 per year in Rhode Island.¹ (Since then lung cancer mortality has slightly overtaken breast cancer mortality among Rhode Island women.) Although breast cancer cannot yet be pre-

Table 2. Screening Recommendations

Breast Cancer

Women 50 years of age and over should be screened by physical examination of the breasts every year and by mammography every year.

Women 40-49 years of age should be screened by physical examination of the breasts every year and by mammography every one to two years.

Women 35-39 years of age should be screened by physical examination of the breasts every year and by mammography once between the ages of 35 and 39, to establish a baseline for the interpretations of later mammograms.

Cervical Cancer

Women younger than 18 who have been sexually active and all women 18 years of age and over should be screened by cervical cytology (Pap smear) every one to three years.

Oral Cancer

Oral cancer screening should be performed by all health professionals who do oral exams, whenever oral exams are performed, especially on *persons 35 years of age and over*. Screening should include thorough visual inspection, including extrusion of the tongue with gauze, looking for changes in color (leukoplakia, erythroplakia), changes in texture (leathery consistency, strawberry/mulberry appearance), changes in continuity (ulcers, lumps), changes in motility (deviations, fixations), followed by palpation of lips, cheeks, tongue, floor of the mouth, palate, salivary glands and lymph nodes (cervical, preauricular, postauricular), focussing special attention on high-risk areas, including the floor of the mouth, lateral borders of the tongue, hard and soft palate, retromolar trigone area including oropharynx, and documentation of the exam in the patient record. Detection of suspicious lesions should result in prompt treatment or referral.

vented, the disease responds well to state-of-the-art therapy when detected early. Unfortunately, only about half the women treated for breast cancer in the US receive such therapy, despite widespread availability.³ If this proportion were increased from 50 to 90%, five-year survival from breast cancer would increase about 9%, according to NCI estimates.³ Accordingly, the Rhode Island Plan's three objectives for the improvement of breast cancer treatment are designed to increase the proportion of women who receive state-of-the-art therapy for breast tumors:

- By 1991, increase the proportion of breast cancer cases staged using AJCC methodology to 100%. (The physician should be responsible for staging a case. The tumor registrar should verify the stage assigned and communicate discrepant findings to the physician).

- By 1991, the proportion of breast cancer cases treated with two-step surgical procedures, biopsy (including fine needle aspiration) with definitive pathology prior to surgery, should increase from 62% to 80%.
- By 1991, the proportion of patients treated according to the recommendations of the Rhode Island Cancer Control Committee (Table 3) should increase to 90%.

Among the recommended actions in the Plan's treatment section is one which grew from comments made at the time of the public hearing. A number of people who testified requested that the Cancer Control Committee address the issue of third-party reimbursement for new cancer therapies which have become medically accepted but are still considered "experimental" or "investigational," some of which are not covered by major health

insurers. In response, the Committee recommended the following action:

- Assess the feasibility of developing a state commission, within the Rhode Island Department of Health, to determine if and when an experimental or investigational cancer drug becomes medically accepted and therefore, should be covered under most health insurance policies.

The Plan also contains a "recommended schema for management of early breast cancer (Stages I and II)," which is displayed in Figure 1.

The Cancer Control Baseline, 1990

Prevention

As Rhode Island enters the 1990s, progress is evident in smoking cessation. The proportion of adults (men and women ages 20 and above) who smoke has declined steadily, from 40% in 1975 to 35% in 1980 to 31% in 1985.⁸ In this period, smoking decreased 26% among adult males, 19% among adult females.

Rhode Island seems to be making progress in smoking prevention among teenagers, as well. In 1975, 33% of teens between the ages of 16 and 19 smoked. In 1980, this figure had dropped to 28%, and by 1985, to 21%. The decline in smoking among male teens, from 34% in 1975 to 18% in 1985, has outstripped the decline in smoking among female teens, from 33% to 23%, but the trend is downward for both sexes.⁸

Additional surveillance of the Rhode Island diet is needed to plan interventions for the prevention of colo-rectal cancer. Past surveys of the Rhode Island population have not assessed diet, because the cost of doing so is high. We do know, however, that 23% of adult Rhode Islanders

Table 3. Treatment Recommendations for State-of-the-Art Breast Cancer Staging and Treatment as of June 1989.

Disease Staging Examinations

Recognizing that patients present with a variety of manifestations, the actual sequence of examinations for staging breast cancer may vary. The following assumes that tissue diagnostics and ER (estrogen receptor) and PR (progesterone receptor) status have been determined. The following staging examinations are suggested for all patients with breast cancer: physical examination, bilateral mammography, usual admission clinical laboratory testing, including alkaline phosphatase and CEA (carcinoembryonic antigen), and chest x-ray. A bone scan is suggested for patients with advanced local disease (T-3, T-4), lymph node metastases (N-1, N-2, N-3), distant metastases, elevated alkaline phosphatase, or bone pain. Liver imaging, i.e., CT scan or isotopic exam, is suggested for patients with elevated alkaline phosphatase or hepatomegaly.

Management of Cases, Stage I, II, and III

All women with operable breast cancer should be considered for adjuvant systemic combination chemotherapy or hormonal treatment depending upon their individual prognostic features, such as involvement of axillary nodes, receptor status, tumor size, age, menopausal status and possibly tumor markers, unless there are medical or psychiatric contraindications present to preclude these options. In view of rapidly developing scientific information, this recommendation should be reassessed at frequent intervals.

Management of Cases, Stage IIIB and IVA

All women with locally advanced breast cancer should be considered for multidisciplinary management with hormonal and/or cytotoxic chemotherapy followed by radiation and/or surgical resection depending upon the feasibility of providing more effective disease control. In view of rapidly developing scientific information, this recommendation should be reassessed at frequent intervals.

were overweight (exceeded ideal body weight by at least 20%) in 1989. With a recent grant from the CDC, the Rhode Island Department of Health has just fielded a small (N=800) statewide survey of food choice. The Department may also include a module of diet questions in its 1990 statewide health interview survey.

Screening

The proportion of women ages 40 and above who have been screened for breast cancer according to current guidelines increased dramatically in the 15 months following the establishment of the Rhode Island Breast Cancer Screening Program, from 30 to 41%. In early 1989, 46% of women ages 40 and above had received either a screening mammogram or a diagnostic mammogram in the past year.⁹

Although many Rhode Island women are properly screened for

cervical cancer, others are not. In 1987, 13% of women ages 20 through 39 had not had a Pap test in the past three years, and 24% of women ages 40 through 69 had not had a Pap test in the past three years, the maximum screening interval recommended for cervical cancer.¹⁰ (The American College of Obstetricians and Gynecologists recommends a screening interval of one year).

Information is needed on the extent of oral cancer screening in Rhode Island. Questions are being designed for the 1990 Rhode Island Health Interview Survey which would measure the proportion of the Rhode Island population who have been screened recently for oral cancer, the setting in which the screening took place, and the procedures used. Analysis of these data will focus on people at high risk of oral cancers, such as people who smoke or chew tobacco.

Treatment

Therapy for breast cancer could be improved for many patients in Rhode Island. In 1986, an estimated 30% of new breast tumors were not staged using the methodology of the American Joint Committee on Cancer (AJCC). In 1985, about four out of ten mastectomies performed at one of Rhode Island's teaching hospitals included biopsy and mastectomy in the same surgical episode. From 1983 to 1986, roughly half the patients diagnosed with stage II breast cancer did not receive chemotherapy.

Comprehensive statewide data on the management of cancer patients are currently unavailable. Estimates must be developed to monitor the application of state-of-the-art therapy over time.¹¹

The Need for Organized, Community-Based Efforts

Organized, community-based efforts have a central place in cancer control. No single organization, or profession, or community has sufficient resources to control this complex problem. Even modest cancer control programs require planning, medical expertise, community organization, public relations, and evaluation. Furthermore, important cancer control issues, such as smoking cessation and diet modification, are also important issues in the control of other major chronic illnesses, such as cardiovascular disease and diabetes. Thus, collaborative ties are important not only among organizations dedicated to cancer control, but also with organizations dedicated to the control of other chronic illnesses.

The Key Role of Physicians

The collaboration and leadership of physicians is essential in all areas of cancer control: prevention, screening, and treatment. Physicians regularly guide their


```

graph TD
    Start([Patient Seeks Medical Attention]) --> D1{Pt. Feels a Mass}
    D1 -- yes --> D2{MD Feels a Mass}
    D1 -- no --> D2
    D2 -- yes --> B1[Surgical Referral History & Physical "Clinical" Staging size, location nodes]
    D2 -- no --> D3{Mammogram Positive}
    D3 -- yes --> B1
    D3 -- no --> End1((Medical Follow-up))
    B1 --> D4{Biopsy Positive}
    D4 -- yes --> B2[Histology, grading and ER/PR If Available: Flow Cytometry S-Phase Analysis]
    D4 -- no --> End2((Medical Follow-up))
    B2 --> B3[Multidisciplinary Consultation Medical Oncologist Radiation Oncologist Plastic Surgeon Oncology Nurse Social Worker]
    B3 --> D5{Further Staging and Workup CBC, LFTs, Chest X-Ray if Indicated: Bone, Liver, or Brain Scans}
    D5 --> D6{Surgery v.s. Radiation}
    D6 -- radiation --> B4["Lumpectomy" and Auxiliary Dissection]
    D6 -- Surgery --> B5[Modified Radical Mastectomy]
    B4 --> D7{Nodes Involved}
    B5 --> D8{Nodes Involved}
    D7 -- yes --> B6[Chemotherapy and/or Hormones]
    D7 -- no --> B7[Radiation Therapy]
    D8 -- yes --> B6
    D8 -- no --> B8[Consideration of Systemic Therapy]
    B6 --> End3((Oncologic Follow-up))
    B7 --> End4((Oncologic Follow-up))
    B8 --> End5((Oncologic Follow-up))
  
```

Most patients trust that physicians will advise them to get the screening tests they need. In a recent survey, for example, 60% of Rhode Island women age 40 and over who had ever received a physician's recommendation for mammography had had a mammogram in the past year, versus 8% who had never received a physician's recommendation.⁹ Furthermore, many primary care physicians perform three of the

Finally, physicians hold the key to state-of-the-art therapy. Physicians recommend, orchestrate, and administer cancer treatments in a complex medical environment. Cancer patients and their families, characteristically stressed and confused, need access to caring, informed physicians to help make critical decisions.

One of the most formidable cancer control challenges to physicians today, and one which will become more difficult in the future, is planning, coordinating, and administering multi-modal

Summary

Rhode Island has one of the highest cancer mortality rates in the nation. In an average year, about 5000 new cancers are reported to the Rhode Island Cancer Registry, and more than 2300 Rhode Islanders succumb to the disease. In response to this problem the Rhode Island Department of Health assembled cancer experts from around the state to plan priority cancer control activities for the 1990s. Their plan for 1990-1992 is the subject of this report.

Five cancers were selected as the foci of cancer control activities: cancers of the lung, colon-rectum, breast, cervix, and oral cavity. The plan proposes prevention, screening, and treatment interventions to reduce morbidity and mortality from these diseases. Rhode Islanders will have to work together to achieve the 33% reduction in cancer mortality proposed as a goal for the year 2000. Surveillance suggests progress on some fronts, but marching in place on others.

References

- ¹ Rhode Island Department of Health: Cancer Rhode Island 1987. Providence, RI: Rhode Island Department of Health, 1989.
- ² Fulton JP, Buechner JS, Baker RS, Tierney JT, Scott HD. Cancer in Rhode Island, an old urban state. Rhode Island Med J 71:139-146, 1988.
- ³ National Cancer Institute: Cancer Control Objectives for the Nation: 1985-2000. Bethesda, MD: US Department of Health and Human Services, Public Health Service, National Institutes of Health, 1986; DHHS publication no. (NIH) 86-2880. (NCI monograph no. 2).
- ⁴ Doll R, Peto R: The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. JNCI, 66(6):1192-1308, 1981.
- ⁵ Rhode Island Cancer Control Committee: Cancer Control Rhode Island, Plan for 1990-1992. Providence, RI: Rhode Island Department of Health, 1990.
- ⁶ Model Standards Project Work Group: Model Standards: A Guide for Community Preventive Health Services. Second Edition. American Public Health Association, Washington, DC, 1985.
- ⁷ Rutstein DD, Berenberg W, Chalmers TC, Child CG, Fishman AP and Perrin EB: Measuring the quality of medical care (second revision of tables, May 1980), a clinical method. NEJM 294:582-588, 1976.
- ⁸ Freedman BE: Report from the 1985 health interview survey: cigarette smoking in Rhode Island. Office of Data Evaluation Newsletter. Providence, RI: Rhode Island Department of Health, October 1986.
- ⁹ Buechner JS, Fulton JP, Feldman JP, DeBuono BA, Kovenock D: Trends in breast cancer screening — Rhode Island 1987-1989. MMWR 38(33):569-571, 1989.
- ¹⁰ Kaufmann RB, Fulton JP, Simon P, Buechner JS, Cody A, Scott HD: Cervical cancer control — Rhode Island. MMWR 38(38):659-662, 1989.
- ¹¹ Cancer Treatment Subcommittee of the Cancer Care Committee: Draft Interim Report: November 1988. Providence, RI: Rhode Island Department of Health, 1988.
- ¹² Schwartz JL: Review and evaluation of smoking cessation methods: the United States and Canada, 1978-1985. NIH Publication No. 87-2940. Bethesda, Maryland: National Cancer Institute, 1987.

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Mammography Referral Patterns Among Rhode Island Physicians

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**Approximately one woman
in ten will develop breast
cancer in her lifetime.**

Introduction

Breast cancer, the most common type of cancer among US women, is second only to lung cancer as a cause of cancer death. Approximately one woman in ten will develop breast cancer in her lifetime. In Rhode Island, there is

reason to be particularly concerned about breast cancer since even with an incidence rate that is 9% lower than that of the US, the mortality rate is 7% higher.¹ In 1989, Rhode Island ranked second in the nation for breast cancer mortality.²

Risk factors for breast cancer have been fairly well delineated³ and include 1) advanced age, 2) history of breast cancer in a first degree relative, 3) personal history of breast carcinoma, or dysplastic breast disease, 4) early menarche, 5) late menopause, 6) first childbirth at age after 30, 7) nulliparity, 8) previous high levels of chest radiation, 9) obesity and 10) high fat diet. Controversy still exists about the role of oral contraceptives and alcohol use. Unfortunately the first 5 and probably the 6th and 7th risk factors are impossible or impractical to modify. The potential for primary prevention of breast cancer through alterations in diet and environment is still an open question.

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ABBREVIATIONS USED:

ACS: American Cancer Society
AMA: American Medical Association
CBE: clinical breast examination
RIBCS: Rhode Island Breast Cancer Screening Program
SBE: self breast examination

Consequently, reductions in breast cancer mortality are best achieved by secondary prevention, ie, early detection of lesions. Methods of early detection include self breast exam (SBE), clinical breast exam (CBE) and screening mammography. Yet despite American Cancer Society (ACS) recommendations for regular screening with breast exams and mammography, only about 40% of women nationally and 70% of women in Rhode Island had had a breast exam within the past year, and only 30% of women nationally and 36% of women in Rhode Island had had a mammogram within the past year.^{4, 5, 6}

Fortunately, within the last decade there has been increasing awareness of breast cancer in the US. Twelve national organizations now recommend screening mammography annually or biennially for women age 40-49 and annually beginning at age 50. The American Cancer Society continues to recommend a baseline mammogram between age 35 and 40. A majority of states currently have legislation mandating some type of insurance coverage and/or quality assurance standards for mammography. In addition, there has been increased attention focussed on breast cancer in the media.

Women themselves and their physicians play a role in insuring that screening is accomplished. Several surveys have delineated barriers perceived by both women and physicians to screening in general and mammography in particular.^{4, 7, 8} Nationally and in Rhode Island, the second common reason women cite for not having a mammogram is lack of physician recommendation.^{4, 9} Therefore, in 1987, in order to determine Rhode Island physicians' knowledge, attitudes and behavior regarding breast cancer screening, particularly mammog-

raphy, we conducted a survey of Rhode Island primary care physicians and compared their responses with physicians nationally. Given the high breast cancer mortality rate and the less than optimal mammography screening rate in Rhode Island, we felt this information would be helpful in developing public health campaigns aimed at overcoming barriers to mammography referral.

Methods

In the fall of 1987, 300 primary care physicians with practices in Rhode Island were surveyed by telephone to measure their agreement and compliance with ACS guidelines for cancer screening. Three updated lists of physicians were obtained from the American Medical Association (AMA): 1) general/family practitioners, 2) general internists and 3) obstetrician/gynecologists. Names were sampled randomly from the three lists, with the objective of interviewing 100 physicians from each. Over the course of one month, 300 physicians were interviewed: 89 general and family practitioners, 134 general internists and 77 obstetrician/gynecologists.

The interview form contained questions used by the ACS in a nationwide survey of primary care physicians in 1984. The Rhode Island survey was conducted by the same firm that conducted the nationwide survey for the ACS. Most of the 1984 questions were asked in Rhode Island, but a few were dropped to reduce survey costs. Questions were used to ascertain attitudes towards ACS guidelines, compliance with them and reasons for not complying.

Aggregate responses from the 1987 Rhode Island survey and 1984 and 1989 US surveys were standardized to the distribution of specialists found in the 1989 US survey, to make them comparable. The proportions of gen-

eral/family practitioners, general internists and obstetrician/gynecologists surveyed in 1989 were used as weights for responses from the 1984 and 1987 surveys. All data in Tables 1 through 5 have been weighted accordingly. The data in Table 6, stratified by physicians specialty have not been weighted.

Weighted frequency distributions and cross tabulations were constructed from individual responses to the 1987 Rhode Island survey. Comparable statistics were constructed by weighting aggregate data from the 1984 and 1989 ACS surveys, originally presented by physician specialty.

Results

In the 1984 national physician survey, only half the respondents reported that they ever ordered mammograms in asymptomatic women with no family history of breast cancer. Conversely, breast physical exam in asymptomatic women was almost universally accepted. In 1987, most Rhode Island physicians accepted mammography as a screening test, as did physicians nationally in 1989.

Despite the same level of general acceptance of mammography by Rhode Island physicians and their colleagues nationally, the two groups reported different influences on the decision to order mammograms for asymptomatic patients. Rhode Island physicians were less likely than physicians in the United States as a whole to report that their decisions were influenced by cost, reliability, safety, sensitivity or availability of mammographic services.

The ACS guidelines recommend screening mammograms biennially for women 40-49 years of age and annually for all women 50 years of age and over, in addition to annual CBE. To measure adherence to this recommenda-

Table 1. Percent of physicians who report that they ever order a mammogram or perform a clinical breast exam for an asymptomatic patient with no family history — Rhode Island, 1987 and United States, 1984 and 1989.

	US 1984*	RI 1987*	US 1989
Mammogram	50	94	96
Clinical Breast Exam	97	98	98

*Standardized to distribution of specialties in US 1989 survey.

Table 2. Influences on the decision to do a screening mammogram in an asymptomatic patient among physicians who ever order screening mammograms — Rhode Island, 1987 and United States, 1989.

	RI 1987	US 1989
Patient can afford	**	53
Cost to patient	18	47
Reliability of mammogram	8	42
Availability of qualified radiologist	14	29
Low chance of finding positives	4	26
Exposure to radiation	8	17
Availability of dedicated machine	4	16

** Not available

Table 3. Percent of physicians who follow or exceed American Cancer Society guidelines for breast cancer screening with all patients — Rhode Island, 1987 and United States, 1984 and 1989.

	US 1984	RI 1987	US 1989
All Physicians Surveyed			
Mammography	11*	43*	37
Clinical Breast Exam	80*	97*	80
General & Family Practitioners			
Mammogram	9	28	34
Clinical Breast Exam	77	96	76
General Internists			
Mammogram	9	44	37
Clinical Breast Exam	76	96	73
Obstetricians/Gynecologists			
Mammogram	17	78	42
Clinical Breast Exam	93	100	89

*Standardized to distribution of specialties in US 1989 survey.

tion, the survey asked physicians what proportion of their eligible patients had been screened with CBE or referred for mammogram. Those who reported that they had ordered mammograms and had physically examined the breasts of 100% of their asymptomatic female patients age 40 and above were considered to be following the guidelines. In 1984, while 80% of physicians surveyed nationally reported that they used CBE to screen for breast cancer in all of their female patients age 40 and over, only 11% reported using screening mammography in all eligible women. In 1987, virtually all Rhode Island physicians surveyed used breast physical exam in all women 40 and over, and 43% reported ordering screening mammograms for all eligible patients, almost four times the proportion in 1984. Nationally, the percentage of primary care physicians who reported doing breast physical exams according to ACS guidelines did not change between 1984 and 1989, but there was a more than three-fold increase in the proportion following the guidelines for screening mammography.

In 1987, general and family practitioners and general internists in Rhode Island were more likely to use CBE in asymptomatic patients than were their national colleagues in both 1984 and 1989. While Rhode Island general internists were more likely than internists nationally to order screening mammograms in both 1984 and 1989, Rhode Island general and family practitioners in 1987 lagged behind their national colleagues in 1989. Obstetrician/gynecologists nationally and in Rhode Island were the most likely group to have accepted and used both these screening tests according to ACS guidelines. This finding was especially true for Rhode Island obstetrician/gyne-

cologists, 78% of whom reported following the guideline for mammography and 100% of whom reported following the guideline for CBE.

In 1984, only 41% of US physicians reported complete agreement with the ACS breast cancer screening guidelines. The remaining 59% reported partial or complete disagreement. In 1987, fully 71% of Rhode Island physicians reported complete agreement, nearly the same as was found nationally in 1989.

Among US physicians in 1984, the most common reason for disagreeing with the mammography guidelines was that the test was too expensive, with fully 39% of physicians citing cost as a factor. This percentage dropped to 18% in 1989. By contrast, in 1987 only 2% of Rhode Island physicians cited cost as a reason for disagreement. In all three surveys, about one quarter of physicians responding disagreed with the ACS guideline on the basis of the recommended frequency of mammography. In 1984 and 1989 a significant number of US physicians disagreed with guidelines because they felt mammograms were not needed if the patient had no symptoms or no family history of breast cancer, or because the yield from mammography was low. While these three issues decreased in importance among US physicians between 1984 and 1989, they were of little or virtually no concern to Rhode Island physicians in 1987.

A large majority of physicians surveyed in Rhode Island and in the United States in 1989 reported that they were more inclined to order a screening mammogram than they had been five years earlier. In both surveys, "satisfactory yield" was most commonly cited as the reason for this increased tendency. "Patient acceptance"

and "reliability of tests" influenced national physicians somewhat more than Rhode Island physicians; "ACS recommendations and guidelines" influenced each group equally.

The estimated number of mammograms ordered in a typical month by Rhode Island physicians as a whole, and Rhode Island physicians broken down by specialty, was nearly identical to the number estimated by US physicians as a whole and by specialty. The number of screening mammograms as a proportion of total mammograms was generally above 75%, but ranged from 69% to 94%, with general internists ordering the highest proportion of screening mammograms.

Discussion

According to women, a physician's referral for a mammogram plays a critical role in whether they have one. In fact, a 1987 survey showed that 60% of Rhode Island women whose physicians recommended having a mammogram subsequently had one, compared with 8% of women with no physician's recommendation. Since physician referral is key to ensuring screening, we have attempted to understand what barriers Rhode Island physicians perceive in following screening guidelines.

In reviewing the data, three limitations must be understood. First, despite existing ACS guidelines for breast cancer screening, it was not until July, 1989 that 12 national organizations including the American Cancer Society, the National Cancer Institute and the American Medical Association agreed on consensus screening guidelines for women 40 and older. Second, the data cited in this article are based on physician self-report which may yield higher numbers for CBE and

mammography referral than actual chart review. Third, we cannot assess changes in behavior among Rhode Island physicians, since the only Rhode Island-specific physician survey was done in 1987. Nevertheless, some important conclusions can be drawn from these data.

Clearly, in 1987, the percentage of Rhode Island physicians who ever ordered a mammogram was significantly greater than the 1984 national percentage, and virtually equal with the 1989 national percentage. This suggests that Rhode Island physicians' acceptance of the value of mammography may have developed earlier than that of their national colleagues. Even in 1987, Rhode Island physicians cited fewer barriers to screening mammography in asymptomatic women than did their national colleagues in 1989. In fact, issues relating to cost, reliability and availability of screening mammography, which were significant problems for physicians nationally even in 1989, were of little or almost no concern to Rhode Island physicians in 1987. It is plausible to attribute some of this disparity to the Health Department's Rhode Island Breast Cancer Screening Program (RIBCSP) which provides access to low cost quality mammography. Although the program itself was not fully operational until November, 1987, intense groundwork for the program was being laid in the year prior to the survey. In addition, the Radiological Society of Rhode Island has taken a very active position on quality assurance for mammography, and it is very likely that their work has been influential in instilling confidence in mammography in Rhode Island physicians as a whole. The lack of confidence by physicians nationally in the quality of services available to them is disturbing, and underscores the need for

Table 4. Percent of physicians who agree or disagree with the American Cancer Society's breast cancer screening guidelines and reasons for disagreement — Rhode Island, 1987 and United States, 1984 and 1989.

	US 1984	RI 1987	US 1989
Agree Completely	41*	71*	72
Disagree	59*	29*	28
Reasons for Disagreement			
Age of baseline too early	**	**	35
Annual testing too frequent	28	23	29
Too expensive	39	2	18
Not needed if no symptoms	29	8	16
Not needed if no family history	14	4	12
Low yield	16	1	9

*Standardized to distribution of specialties in US 1989 survey.

**Not available

Table 5. Percent of physicians who reported that they were more or less inclined to order a screening mammogram than they had been five years earlier — Rhode Island, 1987 and United States, 1989.

	RI 1987	US 1989
Less	1*	0
Same	17*	19
More	82*	81
More Inclined Because:		
Satisfactory yield	26	29
Recommended by ACS and literature	18	18
Reliability of tests	11	17
Acceptance by patients	8	16
Radiation decreased	16	7
Increase in incidence of breast cancer	2	6
To avoid lawsuits	3	6
Availability from local hospital	1	4
Decreased cost	0	3

*Standardized to distribution of specialties in US 1989 survey.

Table 6. Number of mammograms that physicians report they order in a typical month — Rhode Island, 1987 and United States, 1989.

	RI 1987	US 1989
All Physicians Surveyed		
Screening Mammograms	18	18
Total Mammograms	21	20
General & Family Practitioners		
Screening Mammograms	11	13
Total Mammograms	14	15
Internists		
Screening Mammograms	15	16
Total Mammograms	17	17
Obstetrician/Gynecologists		
Screening Mammograms	33	32
Total Mammograms	38	38

the quality assurance initiatives being undertaken by the American College of Radiology and the federal government.

As noted, the number of physicians nationally and locally who order screening mammograms on 100% of their patients according to ACS guidelines, is significantly lower than the number who ever order screening mammograms. Clearly and understandably, physicians feel that screening may not be appropriate for each and everyone of their patients. Despite the low overall rates, in 1987 Rhode Island physicians surpassed their national colleagues for referral according to ACS guidelines. Further, even though physicians nationally reported an increase in adherence to ACS guidelines between 1984 and 1989, they still lagged behind Rhode Island physicians in virtually every specialty. This disparity is consistent with the fact that physicians nationally cite more barriers to mammography than Rhode Island physicians.

Both the national survey and the survey in Rhode Island indicate that even though a large percentage agree with recommended guidelines, many physicians do not recommend mammography to all their patients. As noted earlier, it is understandable that physicians feel that screening may not be appropriate for each and every woman 40 and older. The most obvious reason is that there are some patients for whom mammography would never be appropriate, either due to comorbidity or to the patients' expressed reluctance or refusal to have treatment even if a malignancy were found. Second, without doubt some providers forget to recommend mammography even when such a recommendation would be appropriate, and in the context of a busy practice there is often not adequate time to address this pre-

ventive care issue. Third, in these days of fragmented care, it is likely possible that some providers do not assume responsibility for long term preventive care for patients whom they see only episodically. It is not surprising then that some women report several visits to physicians each year, but do not recall that screening for breast cancer was ever mentioned. To the extent that the third reason results in women not being screened, primary care providers and public health officials must find ways to assure essential screening tests for all eligible women.

More puzzling, however, is the frequency with which physicians report performing clinical breast exams in their patients. Rhode Island physicians utilized CBE in virtually all patients. Nationally, in contrast, physicians utilized clinical breast exam less often, and there was no *change* in utilization between 1984 and 1989, despite the large increase in the use of mammography. The survey questions do not enable us to understand these differences fully, but some possibilities can be considered. One may speculate that increased awareness of breast cancer screening in the mid-1980s focussed on the effectiveness and technological advancements in mammography. In addition, there was an increase in legislatively mandated mammography insurance coverage throughout the country at this time. Thus, this emphasis on mammography could be responsible for the national increase in mammography use between 1984 and 1989, and the lack of emphasis on CBE relative to mammography may have allowed physicians nationally to believe that no change in their behavior regarding CBE was necessary.

However, this difference in emphasis does not explain why

Rhode Island physicians use CBE more frequently than their colleagues nationally (97 vs 80%). It is possible that long-standing primary care training programs in the state have been influential in the adoption of CBE (traditionally considered a standard part of routine gynecologic care), by primary care physicians. It is less clear however why obstetrician/gynecologists nationally perform CBE less frequently than their colleagues in Rhode Island.

As Table 5 shows, "satisfactory yield" is the major reason for increased mammography referral, nationally and locally. Interestingly, although 1 in 10 women in her lifetime will ultimately develop breast cancer, in a population of women who have never been screened mammographically one would expect to find only 5-7 cancers for every 1000 women screened, and in a population of women who have been screened regularly, the yield drops to 3 per 1000. Although this yield is relatively low, the perception of satisfactory yield may again reflect an increased confidence in the quality of mammography in general.

Particularly interesting is that while physicians nationally in 1984 felt cost to be a significant reason for not ordering a mammogram, by 1989 they had significantly increased their rate of ordering, despite the fact that they still perceived cost to be a major barrier to patients. Perhaps physicians feel that the quality and reliability of mammograms have improved enough to override the cost issue. Also possible is that the perception of an increased vulnerability to malpractice suits has influenced their decisions. Whatever the reasons, it is particularly disturbing that cost continues to be perceived as a major issue since more than half of the states have some type of coverage

for screening mammography. This underscores the need for broader coverage of screening mammography and fortunately the mammography benefits contained in the repealed Medicare Catastrophic Coverage Act have been restored.

In summary, while physicians in Rhode Island and nationally appear to agree equally with the American Cancer Society breast cancer screening guidelines, Rhode Island physicians report following those guidelines to a greater degree than their colleagues nationally. Issues such as cost and availability do not appear to be as much of a problem for Rhode Island physicians; and this may be due to the small size of the state and the availability of adequate numbers of dedicated mammography machines. Concern about quality is less of a problem for Rhode Island physicians and we must credit the Rhode Island Radiological Society for its efforts in quality assurance for mammography. In addition, the Department of Health's great emphasis on breast cancer screening and quality assurance for mammography have served to increase awareness about the need for screening. Since women state that lack of physician's recommendation for mammography is the second most important reason they do not have mammograms, Rhode Island's lead in adherence to ACS guidelines is an encouraging foundation upon which to build increased screening in the state. Nevertheless, although Rhode Island physicians refer for mammography more frequently than physicians nationally, the overall rates of referral are still too low. With more effort, we can come closer to reaching the National Health Objectives for the Year 2000, which call for 80% of women 40 and older to be screened with clinical breast exam and mammogram.

Summary

In 1987, the Rhode Island Department of Health conducted a survey of Rhode Island primary care physicians to determine their attitudes and practices regarding breast cancer screening, particularly their use of clinical breast exam (CBE) and referral for screening mammography, and compared the data with information obtained from primary care physicians in the US in 1984 and 1989. The survey showed that the same percentage of Rhode Island physicians (71%) and physicians nationally (72%) agree with American Cancer Society (ACS) guidelines for breast cancer screening, but Rhode Island physicians refer for mammography (43 vs 37%) and perform CBE (97 vs 80%) according to ACS guidelines more frequently. Cost, reliability and availability were of greater concern to physicians nationally than in Rhode Island. Despite better use of breast cancer screening by Rhode Island physicians, only 43% reported referring for mammography according to guidelines. Since studies indicate that the recommendation of her physician is a key determinant of a woman's decision to have a screening mammogram, physician referral needs to increase in order to meet the Year 2000 Objectives of 80% for screening mammography for women 40 and older.

References

- ¹ National Center for Health Statistics: Health United States, 1987. DHHS Pub. No. (PHS)88-1232. Public Health Service. Washington: US Government Printing Office, 1988.
- ² Centers for Disease Control: Chronic Disease Reports — Deaths from breast cancer among women — United States, 1986. MMWR 38:565-569, 1989.
- ³ Page HS, Asire AJ. Cancer Rates and Risks, 3rd Edition, 1985. US Public Health Service, Hyattsville, Maryland, 1985, pp.77-79.
- ⁴ Centers for Disease Control: State-to-state variation in screening mammograms for women ages 50 years of age and older — Behavioral Risk Factor Surveillance System, 1987. MMWR 38:157-160, 1989.
- ⁵ Centers for Disease Control: Use of mammography for breast cancer screening — Rhode Island, 1987. MMWR 37:357-360, 1988.
- ⁶ National Center for Health Statistics. Health promotion data for the 1990 objectives: estimates from the National Health Interview Survey of Health Promotion and Disease Prevention: United States, 1985. DHHS pub. no. (PHS) 86-1250. Public Health Service. Washington: US Government Printing Office, 1986.
- ⁷ Survey of physicians' attitudes and practices in early cancer detection. CA 35:197-213, 1985.
- ⁸ Cummings KM, Funch DP, Mettlin C, et al: Family physicians' beliefs about breast cancer screening by mammography. J Fam Pract 17:1029-34, 1983.
- ⁹ National Center for Health Statistics: Vital and health statistics: breast cancer risk factors and screening: United States, 1987. DHHS Pub. No. (PHS) 90-1500. Public Health Service. Hyattsville, Maryland, 1990.

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Framework for the Rhode Island Response to the Injury Problem

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Injury, currently the fourth leading cause of death in the United States, accounted for more years of potential life lost before age 65 (YPLL) than any other cause.

In the twentieth century, we have made great strides in controlling infectious disease and, more recently, chronic disease. However, the injury death rate has remained relatively constant since 1900.¹ Injury, currently the fourth leading cause of death in the United States, accounted for more

years of potential life lost before age 65 (YPLL) than any other cause. Heart disease, cancer, and stroke precede it in total numbers of deaths; however, in Rhode Island, injury accounted for 9,849 YPLL in 1988, as compared to 8,108 for cancer, 4,592 for heart disease, and only 916 for stroke.

This is because injury is the primary cause of death for children and young adults aged one to 44 (Fig 1). This premature loss of life among young people, in addition to the burden of morbidity and disability from injury, makes it a particularly compelling public health problem.

Although the treatment of injuries has always been a medical responsibility, prevention has been left primarily to law enforcement, highway safety, mental health, and social service agencies. Public health workers have

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ABBREVIATIONS USED:

CDC: Centers for Disease Control

DWI: driving while intoxicated

MVC: motor vehicle crashes

NHTSA: National Highway Traffic Safety Administration

NIAAA: National Institute on Alcohol Abuse and Alcoholism

YPLL: years of potential life lost before age 65

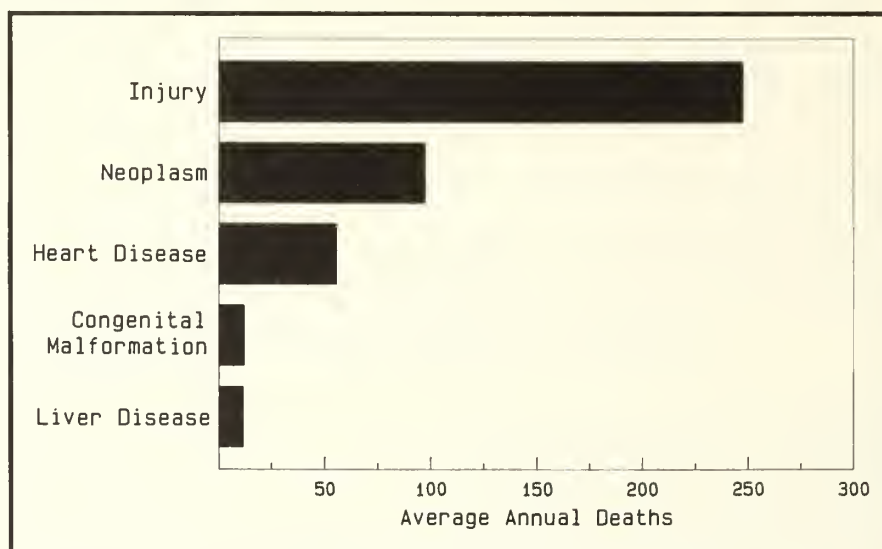
been relatively slow to address the injury problem. However, they are learning that, like diseases, injuries can be studied and prevented by applying an epidemiologic approach.

Risk of injury is related to place of residence, socioeconomic status, the use of alcohol and other drugs, among other factors.

Injury is formally defined as physical damage to an individual due to the transfer of energy (kinetic, thermal, and chemical energy; electricity and radiation) or the absence of essentials for life such as oxygen and heat. Exposure may be chronic or acute. The nature of injuries is diverse, just as there are various neoplasms, for example. Fractures, burns, lacerations, poisonings, suffocations, *et al* are all combined into a single injury category in the International Classification of Diseases.² In order to fully describe injury events, injuries also are classified by how they happened. The cause of injury includes information about the circumstances (fall, slip, crush, etc), the agent (motor vehicle, gun, machine, etc), the location (home, work place, roadway, etc), and whether the event was intentional (eg, homicide) or unintentional (what have traditionally been called "accidents").

Although injury events appear to be different, both intentional and unintentional injuries are studied together because they have common outcomes. (In some cases, as in certain single vehicle crashes, the intentionality of injuries may be difficult to determine.) The epidemiologic distributions of intentional and unintentional injuries are remarkably similar. Both are a significant source of mortality and morbidity

Figure 1. Five Leading Causes of Death in Rhode Island, Ages 1 to 44: 1979-1988



for the young, especially when compared with other health problems. Males predominate in all major injury categories. Risk of injury is related to place of residence, socioeconomic status, the use of alcohol and other drugs, among other factors.

Recent History of Injury Control Efforts in the United States

Accident prevention or safety programs have existed for a long time. However, within the last decade, it became clear that insufficient national attention had been paid to the injury problem. A 1983 law authorized the Secretary of the Department of Transportation to request a study on injury by the National Academy of Sciences. This report, published in May 1985, is entitled *Injury in America: A Continuing Public Health Problem*.³ It describes the breadth of this country's injury problem, outlines the research needs for injury epidemiology, prevention, and biomechanics and makes a clear case for the establishment of a designated center for injury control within the federal government.

In the five years since the pub-

lication of *Injury in America*, much progress has been made toward a structure for national efforts to reduce the injury problem. The Centers for Disease Control (CDC) in Atlanta were designated by Congress to be the location for the injury center. The Center for Environmental Health and Injury Control includes the Division of Injury Control and is responsible for: (1) injury research and the improvement of injury data, (2) training of professionals in the concepts of injury control, (3) promotion of state and local health department injury programs, and (4) coordination of injury control efforts nationwide. Early progress was hampered by limited recognition of CDC's leadership role as well as a lack of resources to accomplish the goals which were set out.

Professionals at a 1985 conference identified the need for a publication directed at injury control practitioners to serve as a companion volume to *Injury in America* which was directed at research needs. *Injury Prevention: Meeting the Challenge*⁴ is the result of a successful collaboration between three federal agencies:

CDC, National Highway Traffic Safety Administration (NHTSA), and the Office of Maternal and Child Health and Resources Development. A multidisciplinary *ad hoc* National Committee for Injury Prevention and Control provided the content for the book. Its members came from public and private organizations and national, state, and local levels of injury practice, research, and teaching. Published in 1989, the book is a practical volume which tells how to design, implement, and evaluate injury prevention programs and describes the current state of knowledge about injury control.

In 1987, Congress directed that a study of injury costs be conducted jointly by NHTSA and CDC. The resulting 1989 report to Congress, entitled *Cost of Injury in the United States*,⁵ was a comprehensive analysis of the fiscal impact of injury and associated disability on this country. Each of these publications has added weight to the argument that more federal resources should be committed to injury control.

Injury prevention finally seems firmly established among national health priorities. The publication this fall of *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*⁶ documented that it is a clear priority. This volume, which will guide health policy for the next decade, identifies 22 priority areas of objectives of which Violence and Abusive Behavior (Priority Area 7) and Unintentional Injuries (Priority Area 9), deal specifically with injury problems. Others, including Alcohol and Other Drugs (Priority Area 4) and Occupational Safety and Health (Priority Area 10), have objectives which relate directly to injury control. The objectives for injury present a clear mandate for injury control programs at the state and local level.

History of the Rhode Island Department of Health Response

The Rhode Island Department of Health has been in the forefront of the national effort to promote injury control. The 1988 Harvard School of Public Health's survey of state health departments⁷ reported that Rhode Island was one of 32 states with injury control programs. Historically, most efforts have focused on specific target injuries and/or groups and have involved personnel from various divisions within the department.

The Department of Health has been active in setting injury control policy for many years. Specific injury control agendas were contained in all three State Health Plans (1980, 1983, and 1986)^{8, 9, 10} which were developed by the Statewide Health Coordinating Council. These plans included goals to reduce "accidents" (ie, unintentional injuries), homicide, and suicide and recommended strategies for home safety, transportation safety, occupational safety, and substance abuse prevention. A more recent planning effort on Rhode Island's need for a developed trauma system¹¹ again included recommendations, not just for an improved treatment system, but for the prevention of injuries through legislation.

Rhode Island had some early success in injury control legislation. The Department of Health supported passage of a child restraint law, which passed in 1980, the second such law in the nation. The stress on protection of motor vehicle occupants has continued to the present. In 1983, the Department sponsored a substantial seat belt use policy initiative, and efforts to encourage the use of passenger restraint systems are ongoing. They include the dissemination of educational

materials on passenger restraint systems for adults and children. The planning efforts described previously have led to the development and support of legislation for mandatory seat belt use, mandatory motorcycle helmet use, and stronger laws governing driving while intoxicated (DWI).

Suicide prevention has been a particular focus of the Division of Family Health. A legislative appropriation sponsored by the Lieutenant Governor's Task Force on Teenage Suicide, along with grant money from the New England Network to Prevent Childhood Injury, funded the collection and analysis of Rhode Island Hospital Emergency Department data on adolescent suicide attempters.¹² This effort was a collaboration between the Department of Health, Rhode Island Hospital, and the Brown University Department of Child Psychiatry.

The Rhode Island Department of Health has been successful in obtaining federal support for research and prevention activity on specific injury problems. From 1984 to 1987, NHTSA sponsored emergency department based surveillance of motor vehicle injuries. This allowed for the monitoring of the characteristics of those injured in motor vehicle crashes. The Community Alcohol Abuse/Injury Prevention Project was funded from 1985 to 1989 by CDC and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Follow-up research continues under the sponsorship of NIAAA. This project aimed to measure the effects of programs to reduce alcohol-related mortality and morbidity resulting from assaults and motor vehicle crashes.¹³ In 1989, CDC funded the Rhode Island Department of Health Office of Health Statistics to conduct a project for the surveillance of injury morbidity in

Rhode Island. The project will work to improve the reporting system of hospital discharges for injuries.

To date, the broadest initiative impacting injury in Rhode Island began in 1989 as a program funded for a four-year period by CDC. The Injury Prevention Program is intended (1) to centralize coordination of the various Department of Health injury control functions within the Division of Health Policy, (2) to assess injury information needs, (3) to develop a comprehensive statewide injury control plan, and (4) to implement specific prevention programs. Findings from early work from this project are reported next.

Setting Injury Prevention Priorities for Rhode Island

Priorities for injury control will be based on injury data. Likewise, appropriate interventions will be targeted through evaluation of the distribution of injuries throughout the state. Therefore the assessment of existing injury data sets and the improvement of data quality and accessibility are important functions of the Injury Prevention Program.

Available data sources can provide information essential to injury research, including:

- who is injured (age, sex, race, socioeconomic status)
- when injury events occur (day of week, date, time)
- cause of injury
- location of the injury event (eg, home, work, school)
- risk factor information (eg, use of alcohol or other drugs, safety belt or helmet use)
- severity of injury

Several important sources of injury data are being analyzed by the Injury Prevention Program. Their utility for describing injury,

their comprehensiveness, and their accessibility vary.

Appropriate interventions (for injury control) will be targeted through evaluation of the distribution of injuries throughout the state.

Death certificates provide demographic and cause of death information for all deaths occurring in Rhode Island. While the amount of injury information is relatively limited, the data set is accurate and readily accessible. A study utilizing Rhode Island death certificates will be discussed subsequently.

The *Medical Examiner's Office* investigates all injury deaths occurring within Rhode Island. This highly accurate data set provides more injury information than death certificates; however, the lack of a computerized data base makes access to the information difficult.

Hospital discharge data are highly accessible and provide valuable injury morbidity information. Data are abstracted from discharge records. The recording of external cause of injury (E-codes) will be improved through the efforts of the Injury Surveillance Project.

A *trauma registry* located at the Rhode Island Hospital is currently being developed. In addition to detailed injury information on trauma cases referred to the Trauma Center, the computerized registry will provide measures of injury severity for this important group of hospitalizations.

Emergency departments are potentially an excellent source of injury morbidity information. The data currently are inaccessible, however, since they are not standardized or computerized in most Rhode Island hospitals.

Both mortality and morbidity data are necessary to produce an accurate picture of injuries in Rhode Island. Most people who are injured do not die of their injuries, but suffer a range of injury severity. Mortality may be thought of as the tip of a pyramid. For instance, *Cost of Injury* documents that for every injury death in the US there are 16 hospitalizations and 381 injuries not resulting in hospitalization. Injury morbidity data provide the researcher with more information with which to study the causes and consequences of injury. In addition, the injury problem as portrayed by morbidity data may be substantially different than as seen through mortality data.

Mortality Data Overview

An analysis of ten years (1979-1988) of Rhode Island injury mortality data from death certificates is being completed; this study provides a descriptive epidemiology of injury mortality. The major causes of injury mortality to Rhode Islanders during 1979-1988 are shown in Fig 2. The age and sex distributions for the top four leading causes of death are illustrated in Figs 3-6.

Motor Vehicle Crashes: The injury mortality rate is highest for motor vehicle crashes (MVC): 13 deaths annually per 100,000 population. Victims in this category consist of motor vehicle occupants, motorcyclists, bicyclists, and pedestrians. During the period 1979-1988, there were an average of 125 deaths per year due to MVCs. Fig 3 illustrates that for all age groups males have higher traffic mortality rates than females. Among males, those aged 15 to 24 are at highest risk; mortality rates decrease with increasing age groups until the 65 and over age group. The profile for females is similar, except that women aged 65 and over are most

Figure 2. Leading Causes of Injury Mortality in Rhode Island, 1979-1988

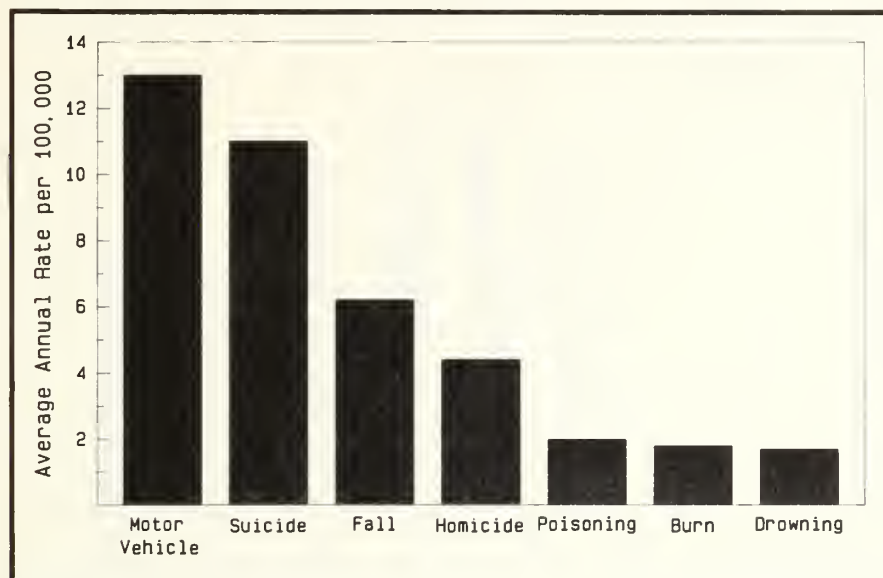
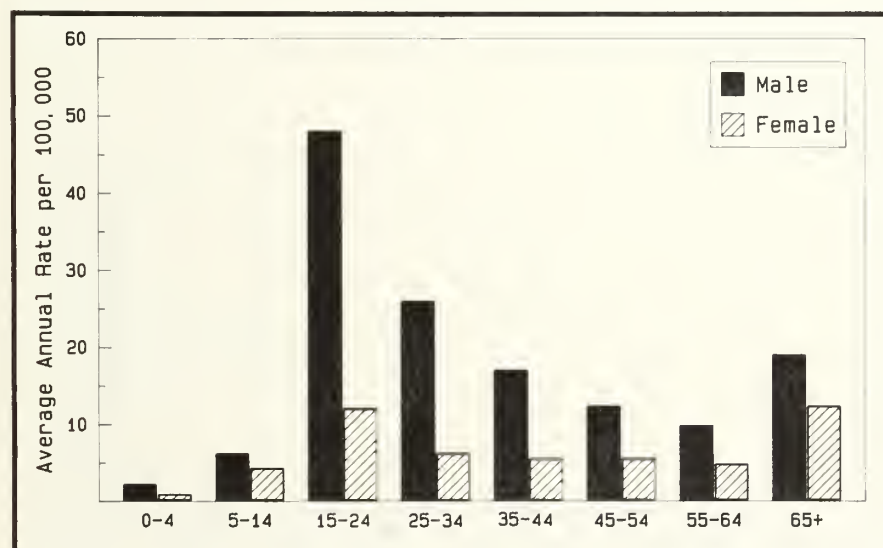


Figure 3. Fatalities from Motor Vehicle Crashes in Rhode Island, 1979-1988



at risk. Additional data on risk factors and health are needed to understand these findings more fully.

Suicide: Suicide is second only to MVCs as a cause of injury death in Rhode Island. The annual number of suicides for the ten year period 1979-1988 was 107. The actual annual average may be higher since suicides are likely underreported. The low rate for children less than fifteen years old

(Fig 4) is misleading since suicides are not rare for those under 10. For all age groups, the rate for males is more than twice that for females; in fact, males aged 15-24 have more than seven times the risk of committing suicide than their female counterparts. At highest risk in Rhode Island are males aged 25-34. Middle-aged women have the highest suicide rate of their gender, moderately elevated relative to other age

groups.

Falls: An average of 60 Rhode Island residents die annually due to falls. As dramatically illustrated in Fig 5, fatal falls occur primarily among the elderly. The rate for those aged 65 and over is 10 times the rate of the next highest group (55-64 age group). Because Rhode Island has a relatively large elderly population, falls are the third leading cause of injury mortality in the state. For almost every age group, the mortality rate for falls is higher for males than females.

Homicide: From 1979 to 1988, an average of 42 Rhode Islanders were murdered annually. As with other injuries, males are at higher risk (Fig 6). The homicide rate is greatest for 25-34 year old men; their rate is more than three times that of women in the same age group. Among females, those aged 15-24 are at highest risk. Following their respective peaks, homicide rates decrease with age for both genders.

Year 2000 Injury Objectives: As has been discussed, the Year Health 2000 objectives set forth specific national objectives for injury prevention to be achieved by the year 2000. Utilizing Rhode Island death certificate data, comparisons can be made with those objectives, and prevention priorities can be determined. Target mortality rates are presented in Table 1 along with the respective US and Rhode Island rates. The state's mortality rates are below the Year 2000 Health Objectives for several injury causes. However, target rates for this state will need to be established in order for us to contribute to meeting the national objective.

The Next Steps

This paper has described some of the important developments in injury control which have occurred. Under the auspices of the

Injury Prevention Program, a planning effort for the Rhode Island Department of Health has begun. An Injury Prevention Planning Committee was appointed by the Director of Health to bring community perspectives to this issue; it began meeting in May 1990. This committee has 16 members, including physicians from a variety of specialties, representatives of state agencies, and representatives of private organizations concerned with injury issues. The committee expects to report recommendations for a planned departmental approach to injury issues early in 1991. Recommendations will undoubtedly address injury data needs, make recommendations for priority areas to be explored for intervention programming and/or legislative approaches, and include the need for a more comprehensive planning process to set specific Rhode Island injury goals for the year 2000.

Activities in Progress: Some activities for the next year have already been identified. The Department of Health will continue to advocate for those legislative actions which have already been endorsed. Such proposed legislation includes a universal mandatory seat belt law, required motorcycle helmet use for all drivers and passengers, and reduced legal blood alcohol content for defining DWI. Injury Prevention Program staff will continue to identify and track all proposed legislation affecting the prevention of injuries in the state. This tracking began in the 1990 legislative session. Information will be regularly shared through the project newsletter, *Injury Information*. There will also be continuing investigation of legislative models from other states as well as the development of new proposals to meet the needs of Rhode Island.

Another clear avenue for inter-

Figure 4. Suicides in Rhode Island, 1979-1988

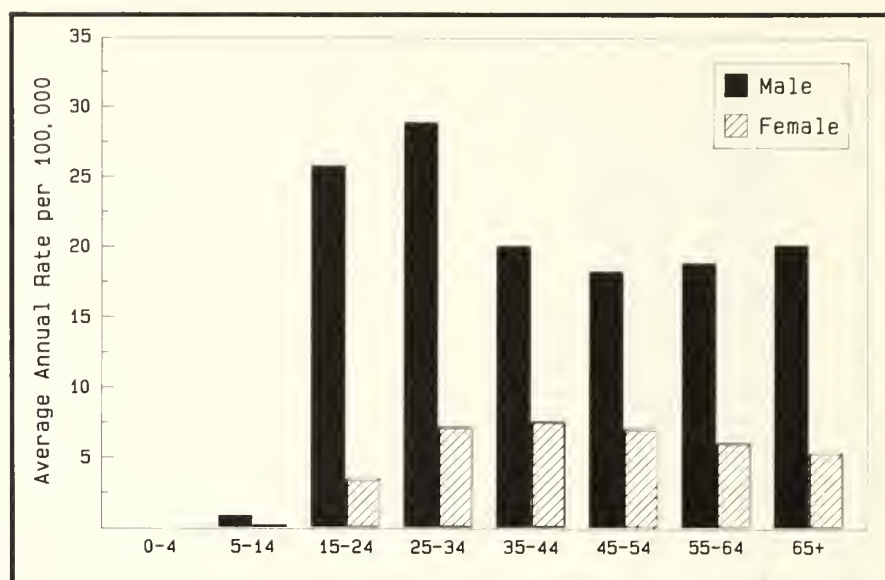
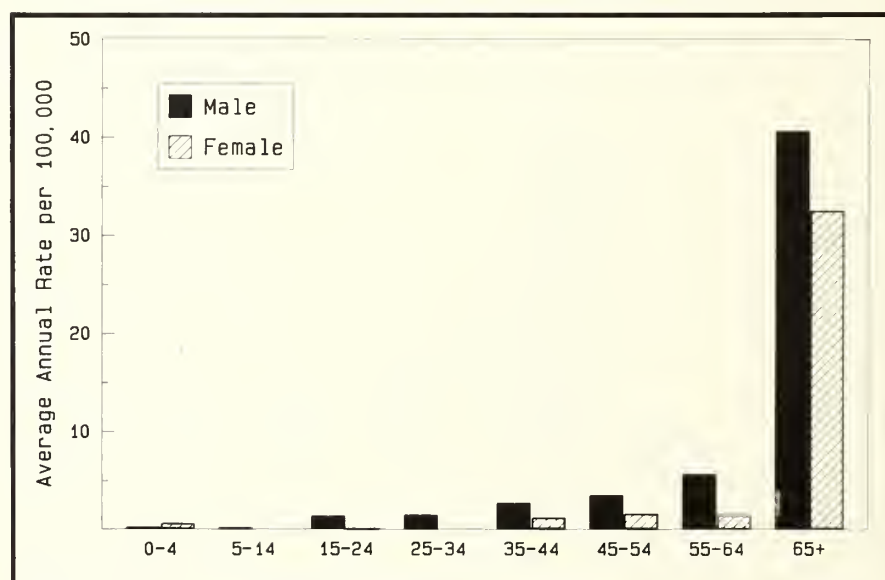


Figure 5. Fatalities from Falls in Rhode Island, 1979-1988



vention is increased enforcement of the many protective laws which already exist. For example, the child safety seat law has existed in Rhode Island for over ten years. However, observation shows that compliance with this law is far from universal. A study done in Tennessee demonstrated that the level of citations issued for non-use of safety seats had a direct

impact on the level of child fatalities occurring in motor vehicles crashes.¹⁴ A review of existing injury-related laws and their current level of enforcement is needed.

Other already identified approaches to injury prevention include environmental modification, product design, and education. All of these are being

Figure 6. Homicides in Rhode Island, 1979-1988.

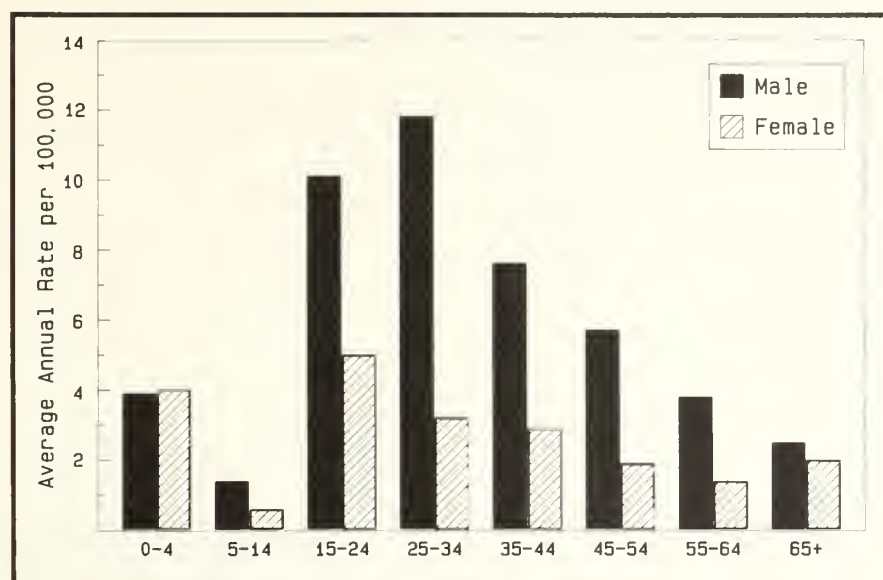


Table 1. National Mortality Objectives for Year 2000 (rates per 100,000)

Injury Cause	1987 U.S.	1984-88 R.I.	Year 2000 Goal
Homicide	8.5	4.4	7.2
Suicide	11.7	10.8	10.5
Motor Vehicle Crash	19.1	13.1	17.0
Fall	2.7	5.4	2.3
Drowning	2.1	1.0	1.3
Fire	1.5	1.5	1.2

Table 2. Rhode Island Department of Health Injury Prevention Planning Committee

Joseph Pfeifer, MD; Chair	Rhode Island Hospital Trauma Center
Stanley M. Aronson, MD	Brown University School of Medicine
Sharon K. Brinkworth	RI Safety Belt Coalition
Karen Costello	American Red Cross Narragansett Bay Chapter
Richard Dvorin, MD	Rhode Island Group Health Assn. Department of Pediatrics
Mel H. Epstein, MD	Rhode Island Hospital Department of Neurosurgery
Esther Giammarco	Department of Education Driver Education Program
James Burns	Fire Marshall's Office
Anthony Maione	The Samaritans
Donald R. Morath, MD	Roger Williams General Hospital
Eugene Nadeau	Dept. of Mental Health, Retardation and Hospitals, General Hospital
Marianne Raimondo	Hospital Association of RI Quality and Information Services
Donna Sassi, RN	RI Emergency Nurses CARE
William Tocco	Johnston Police Department
David M. Trainor	RI State Police
Edward J. Walsh	Governor's Office on Highway Safety

planned to reduce Rhode Island's injury problem. Research has made it clear that the more automatic a protection is the greater chance it has of successfully reducing injury. Traditional safety education approaches should be, in large part, supplanted with interventions which do not rely solely on persuading individuals to do what is best for them. However, educational interventions are also important to implement on the state and local level.

New Initiatives: In the second-year plan for the Injury Prevention Program submitted to CDC, some specific injury control programs have already been identified and funded. They include:

- Training in the public health approach to injury for health professionals
- Conference on Year 2000 Injury Objectives for Rhode Island in Spring 1991
- Speakers bureau to disseminate injury prevention information to consumer groups
- Educational campaign on seat belt use
- Other cooperative projects including a bicycle helmet project, a program to reduce work site injuries, and a violence prevention project.

Many injury control measures are best implemented on a local basis rather than statewide. Therefore, the Department of Health programs will include many community-specific efforts. For example, a summer program in urban areas at high risk for fatal house fires will install smoke detectors in housing units and replace batteries in existing detectors. This program is being designed as an expansion of the existing pediatric lead screening program in the Division of Family Health.

Local solutions for traffic injury problems will be sought through a program of competitive small

grants to community programs; this program is being administered in cooperation with the Governor's Office on Highway Safety. The Injury Prevention Program will provide technical assistance, but the programs will be implemented by people within local communities. At least four projects will be selected in the state to address problems such as bicycle injuries, DWI, and passenger restraint use.

Conclusion

The injury control activities pursued through these short term federal funds, even when added to already established programs, will only begin to impact injury mortality and morbidity. However, they will support the development of an approach which will enable public health to make the same kind of progress on the control of injuries as it did with infectious disease earlier in the century. We expect that the medical community will continue to be key participants in this process and that they will play a leadership role in the injury control movement in Rhode Island.

Summary

Injuries are the fourth leading cause of death in Rhode Island as well as the US and are responsible for the greatest amount of premature death. Recent years have brought more national attention to the role of public health in injury prevention. The Rhode Island Department of Health has been involved in a variety of injury control research, programs and legislation. In 1989, the Injury Prevention Program was funded through a grant from the Centers for Disease Control to coordinate and implement injury control programs in the Department. Injury prevention priorities are set on the basis of mortality and morbidity data. An analysis of Rhode Island

death certificate data from 1979 to 1988 reveals that motor vehicle crashes, suicides, falls, and homicides are the leading causes of injury deaths. Age patterns vary for each cause, but males predominate in all categories of injury deaths. Activities to reduce injuries are underway or planned. Physicians will play key roles in this effort.

References

- ¹ Baker SP, O'Neill B, and Karpf RS: The Injury Fact Book. Lexington, MA: DC Heath and Company, 1984.
- ² Public Health Service: The International Classification of Diseases, 9th Revision, Clinical Modification. Third Edition, Volume 1. DHHS Publication No. (PHS) 89-1260, Washington, DC: US Government Printing Office, March 1989.
- ³ Committee on Trauma Research, Commission on Life Sciences, National Research Council, and the Institute of Medicine: Injury in America: A Continuing Public Health Problem. Washington, DC: National Academy Press, 1985.
- ⁴ The National Committee for Injury Prevention and Control: Injury Prevention: Meeting the Challenge. New York, NY: Oxford University Press, 1989.
- ⁵ Rice DP, MacKenzie EJ *et al.*: Cost of Injury in the United States: A Report to Congress. San Francisco, CA: Institute for Health & Aging, University of California and Injury Prevention Center, The Johns Hopkins University, 1989.
- ⁶ US Public Health Service: Healthy People 2000: National Health Promotion and Disease Prevention Objectives. Conference Edition. Washington, DC: US Government Printing Office, 1990.
- ⁷ Harrington C, Gallagher SS, Burgess LL, Guyer B: Injury Prevention Programs in State Health Departments. Cambridge, MA: Harvard School of Public Health, 1988.
- ⁸ Rhode Island Department of Health: Rhode Island State Health Plan. Providence, RI: Rhode Island Department of Health, 1980.
- ⁹ Rhode Island Department of Health: Rhode Island Health Plan: 1983-1987. Providence, RI: Rhode Island Department of Health, 1983.
- ¹⁰ Rhode Island Department of Health: Rhode Island Health Plan: 1987-1992. Providence, RI: Rhode Island Department of Health, 1986.
- ¹¹ Rhode Island Department of Health: Trauma System Planning Committee Recommendations. Providence, RI: Rhode Island Department of Health, 1990.
- ¹² Ashworth S, Spirito A, Colella A, Drew CB: A pilot suicidal awareness, identification, and prevention program. Rhode Island Med J 69:457-461, 1986.
- ¹³ Harrington CR, Putnam SL, Waters WJ, Colt AM: The community gatekeeper training model for reducing alcohol abuse and alcohol-related injury. Rhode Island Med J 72:459-463, 1989.

¹⁴ Decker MD, Dewey RH, Hutcheson RH, Schaffner W: The use and efficacy of child restraint devices. JAMA 252: 2571-2575, 1984.

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Profiling Motor Vehicle Traffic Trauma in Rhode Island

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For both sexes, ages 15-19 years registered the highest rates of overall motor vehicular trauma . . .

Motor vehicular trauma is the leading cause of injury mortality in Rhode Island,¹ as in the United States.² However, such deaths represent just the tip of the injury iceberg. In order to provide a more comprehensive picture of the road toll and to evaluate countermeasures, principally an anticipated universal mandatory seat belt use law, the Rhode Island Department of Health undertook the first reported investigation of motor

vehicular trauma in the nation to use statewide hospital emergency department data.³ The methodology employed was similar to that used in the Northeastern Ohio Trauma Study.⁴ Complementing a previous report,⁵ this report presents detailed traffic trauma rates by demographic and road-use characteristics, and a comparison of the age-sex composition of total and severe trauma cases, respectively, with that of

the Rhode Island population. The observation period was calendar years 1984 and 1985.

Materials and Methods

Cases comprised a 25% systematic sample of first encounter motor vehicle traffic trauma patients treated during 1984 and 1985 in the emergency department of any of the 12 civilian, acute care, nonpsychiatric hospitals in Rhode Island with such a facility. They further pertained to patients who were Rhode Island residents of known age and sex, and who were or could be assigned an external cause of injury code (E-code) within ranges E810-E816 and E818-E819 according to the ninth revision of the *International Classification of Diseases, Clinical Modification*.⁶ Adhering to the same E-codes, a complete enumeration of traffic fatalities was obtained from official vital records on Rhode Island residents who died as a result of motor vehicular trauma sustained on public roads in Rhode Island within the observation period. The vital records are maintained by RIDH. The study population ($n = 6,268$) was reduced by 0.4% to eliminate

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cases with unknown age or sex.

Numerators in the overall rates were annual averages of motor vehicular trauma occurrence that was estimated from weighted emergency department cases. Weights were the inverse of the sampling fraction; that is, four. Numerators in the severe trauma rates were annual averages of a combination of weighted nonfatal admissions and total fatalities. Again, the weights were the inverse of the sampling fraction. For analysis of severe trauma, which was operationalized as motor vehicular trauma resulting in death or hospital admission, the initial age groups were collapsed due to small numbers. The enlarged categories typically embraced age groups which manifested similar overall trauma rates. Rate denominators were corresponding mid-period age- and sex-stratified population estimates that were derived through linear interpolation, using as referents the 1980 Rhode Island Census population⁷ and an official projection of the State population for July 1, 1985.⁸

In the statistical analysis of overall trauma, which was based just on the 25% hospital emergency department sample, counts were assumed to be distributed as a Poisson. The sample count served as the estimated variance. For the severe trauma analysis, the numbers of fatalities and nonfatal sample hospital admissions were assumed to be independent occurrences, with both distributed as a Poisson. In each analysis, the variance of the estimated rates was calculated using the Poisson variable and appropriate constants. Further methodological information, as on quality control procedures, is available from other sources.^{9, 10}

Results

Overall Trauma

Seventy-five percent of cases in-

Figure 1. Annualized motor vehicular trauma rates by age and sex for persons treated in hospital emergency departments, Rhode Island, 1984-1985.

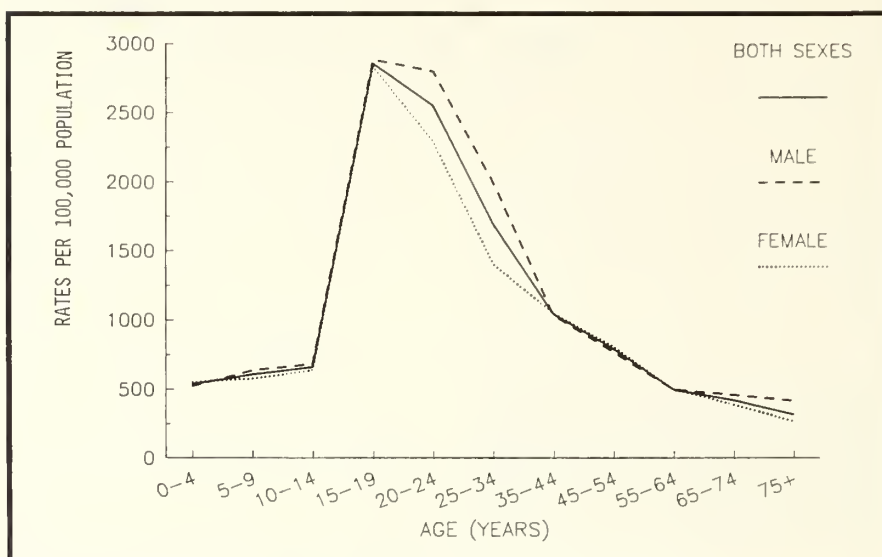


Figure 2. Annualized motor vehicular trauma rates by road-use status, age, and sex for persons treated in hospital emergency departments, Rhode Island, 1984-1985.

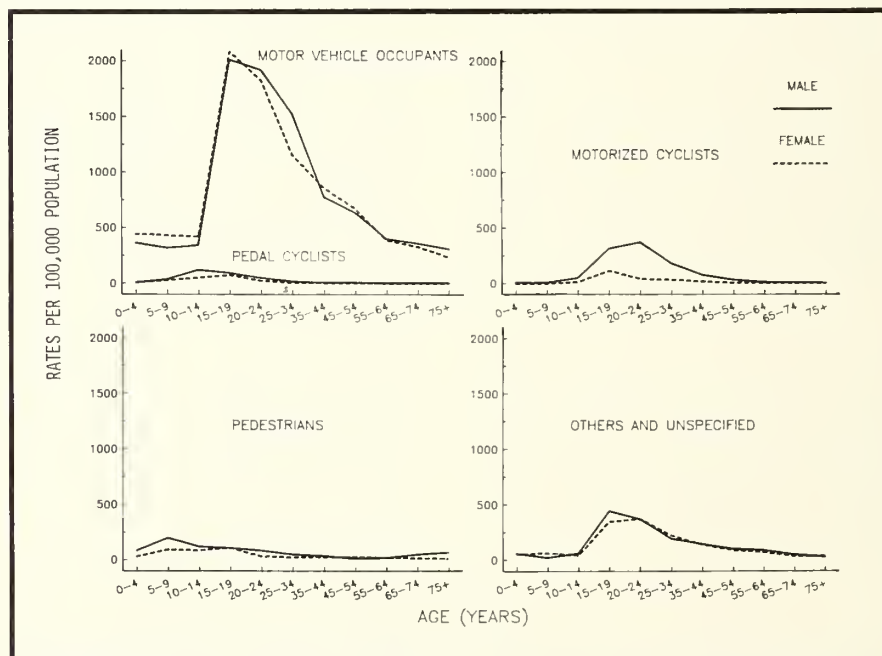


Figure 3. Annualized rates of motor vehicular trauma resulting in death or hospital admission by age and sex, Rhode Island, 1984-1985.

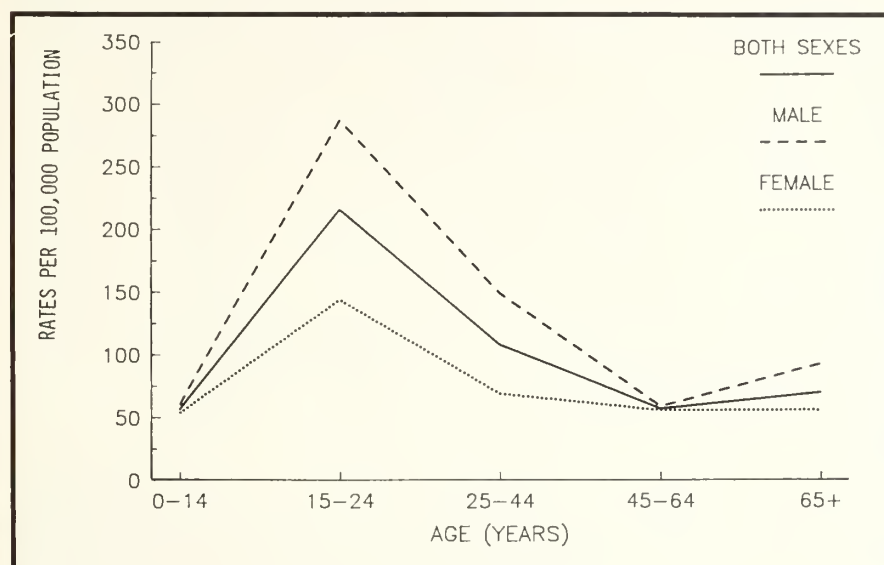
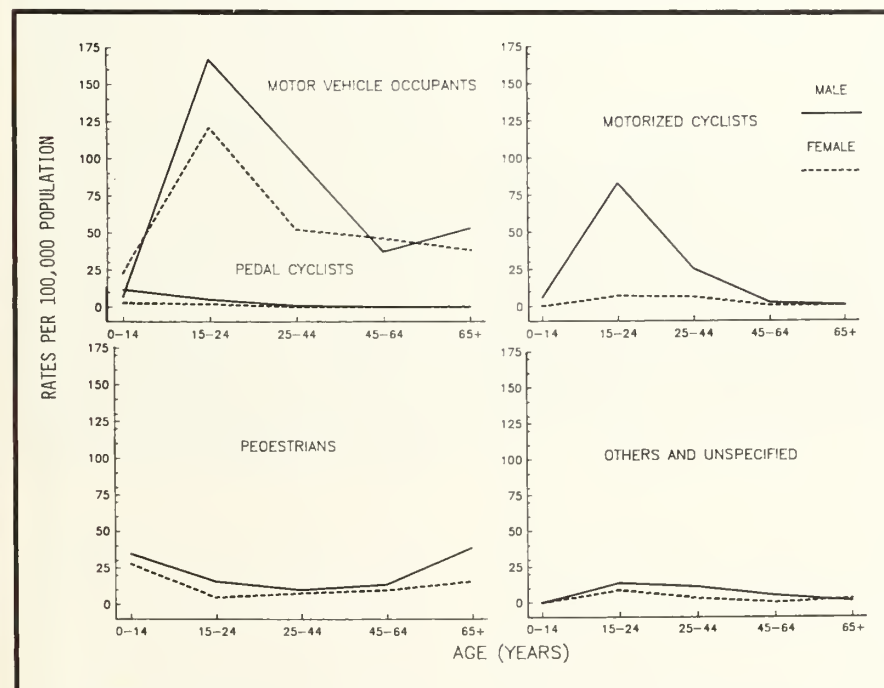


Figure 4. Annualized rates of motor vehicular trauma resulting in death or hospital admission by road-use status, age, and sex, Rhode Island, 1984-1985.



involved the motor vehicle occupant category. For both sexes, ages 15-19 years registered the highest rates of overall motor vehicular trauma for the total (Figure 1), and in the motor vehicle occupant, motorcyclist, and other/unspecified road-use categories (Figure 2). Ages 20-24 years registered the second highest rates by sex, disregarding road-use status. The highest sex- and road-use-specific rates were manifested for males in the motorcycle category. Male rate excesses characterized all road-use categories except other/unspecified, and were particularly pronounced for motorcycle trauma (Table 1).

Severe Trauma

Sixty four percent of severe trauma cases were in the motor vehicle occupant category, with another 29% being classified in either the pedestrian or motorcycle category. The severe trauma rate reached a zenith at ages 15-24 years independent of sex, and was smallest at ages 0-14 and 45-64 (Figure 3). Again independent of sex, the highest rates of severe trauma for three of the road-use categories, namely, motor vehicle occupant, motorcyclist and other/unspecified, occurred at ages 15-24 (Figure 4).

... the largest sex differentials were observed in the motorcyclist category, where there was a nine-fold rate excess for males.

There was an 80% male excess in severe motor vehicular trauma rates (Table 2). At ages 15 through 44 years, males manifested approximately twice the risk of sustaining severe trauma on public roads as females. When road-use status was disaggregated, the largest sex differentials were observed in the motorcyclist cate-

gory, where there was a nine-fold rate excess for males. Between ages 15 and 24, this excess approached 12. A four-fold male excess in rates was evident in the pedal cyclist category. Reversing the usual tendency, females manifested a three-fold rate excess at ages 0-14 years in the motor vehicle occupant category.

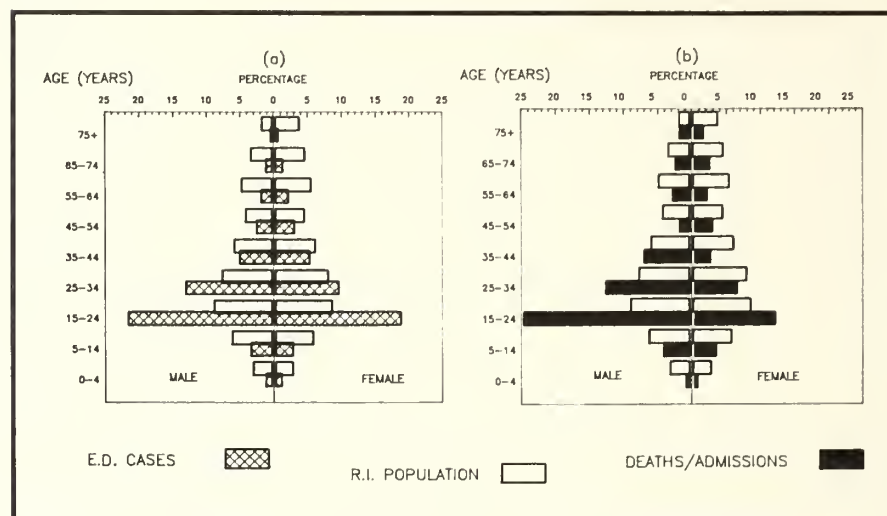
Population Comparisons

Profound demographic differences were evident between the motor vehicular trauma sample and the estimated mid-period Rhode Island population (Figure 5). While only 18% of the State population were aged 15-24 years, they accounted for 41% of estimated total motor vehicle trauma cases and 38% of estimated severe cases. The males alone (9% of the population) produced 22% of former cases and 25% of latter ones. Rhode Island residents of both sexes in the 25-34 age group also were proportionally overrepresented among overall trauma cases, as were males from the same age group among severe trauma cases.

Discussion

Although data were not collected on resident cases involving treatment in out-of-state hospital emergency departments, the numbers of such cases are deemed to be well under 10% of the estimated total. Based on 1982 all-cause data, there were an estimated 107 residents from Massachusetts and Connecticut admitted to Rhode Island hospitals for every 100 Rhode Island residents admitted in those states.¹¹ Out-of-state residents were estimated to constitute 7% of admissions to Rhode Island hospitals with the great preponderance originating in Massachusetts and Connecticut. This figure closely approached the 6% of out-of-state residents estimated to have re-

Figure 5. Composite age-sex pyramids of Rhode Island population and respective estimated resident (a) hospital emergency department motor vehicular trauma cases, and (b) motor vehicular trauma cases resulting in death or hospital admission, 1984-1985.



ceived treatment for motor vehicular trauma in Rhode Island hospital emergency departments during the observation period.

Males with minor injuries are hypothesized to be more prone than their female counterparts to bypass the health care system, including hospital emergency rooms.

Explanation of observed sex differences in motor vehicular trauma rates lies beyond the scope of this report. Nevertheless, the finding that male excesses were much less pronounced in the case of overall motor vehicular trauma than with severe motor vehicular trauma rates invites speculation. While part of the discrepant excesses likely represent real differences, part might be an artifact stemming from the discretionary nature of individual care seeking in

hospital emergency departments when injuries are minor. Males with minor injuries are hypothesized to be more prone than their female counterparts to bypass the health care system, including hospital emergency departments. One rationale is that this avoidance behavior is a product of males having less flexible social roles than females,^{12, 13} and being socialized to be more stoical.^{13, 14} The hypothesis, and supporting alternative rationales, should be tested with appropriate data. Results could have important implications for the absolute and relative magnitude of hospital emergency department-based trauma rates. Just as differential utilization practices would distort gender comparisons of trauma rates, they similarly could affect comparisons concerning other patient socio-demographic characteristics, such as immigration status,¹⁵ race, and social class.^{16, 17}

Even if differential utilization of hospital emergency departments

Table 1. Male to Female Ratios of Annualized Motor Vehicular Trauma Rates by Age, Sex, and Road-use Status for Persons Treated in Hospital Emergency Departments, Rhode Island, 1984-1985†

Age (years)	Road-use Status					Total
	Motor vehicle occupant	Motorized cyclist	Pedal cyclist	Pedestrian	Other/unspecified	
0-4	0.82		0.48	2.66*	0.95	0.95
5-9	0.74		1.44	2.06*	3.21	1.10
10-14	0.82	3.82	2.39*	1.36	0.67	1.07
15-19	0.97	2.76**	1.22	0.98	0.79	1.02
20-24	1.05	9.20**	2.14	2.44*	1.01	1.22**
25-34	1.32**	6.03**	3.67	2.00	1.16	1.42**
35-44	0.90	4.58**	2.08	1.39	0.97	0.99
45-54	0.94	6.55	2.18	0.41	0.86	0.95
55-64	1.03	2.32		1.16	0.79	1.00
65-74	1.09			3.40*	0.68	1.17
75+	1.32			4.88*	1.67	1.55
All Ages‡	1.10**	5.34**	1.97**	1.73**	1.02	1.21**

* $p \leq .05$; ** $p \leq .01$.

† Blank indicates that ratio was not computed because one or both rates equal zero.

‡ Excludes cases with unspecified age or sex.

Table 2. Male to Female Ratios of Annualized Rates of Motor Vehicular Trauma Resulting in Death or Hospital Admission for Persons Treated in Hospital Emergency Departments by Age, Sex, and Road-use Status, Rhode Island, 1984-1985†

Age (years)	Road-Use Status					Total
	Motor vehicle occupant	Motorized cyclist	Pedal cyclist	Pedestrian	Other/unspecified	
0-14	0.30*		4.21	1.26		1.12
15-24	1.39	11.94**	2.19	3.14	1.62	1.99**
25-44	1.94**	4.38**		1.28	3.79*	2.17**
45-64	0.79			1.47		1.05
65+	1.42			2.52	0.32	1.67
All Ages‡	1.40**	9.01**	4.26*	1.63*	2.55*	1.80**

* $p \leq .05$; ** $p \leq .01$.

† Blank indicates that ratio was not computed because one or both rates equal zero.

‡ Excludes cases with unspecified age or sex.

by patient sex were not problematic in this context, the true rates of motor vehicle traffic trauma in Rhode Island still could not be estimated from the available data. Omitted from this study were cases involving the untreated, the self-treated, and those who were treated in out-of-state hospitals, a health maintenance organization, a freestanding clinic, a military facility, or in the office of a physician or some other health

care provider. Since, on average, these injury cases should be less serious than those in this study population, their omission would generate overrepresentation of more severe cases in that population. Given these selection constraints, estimated severe trauma rates will more closely approximate true rates than do overall trauma rates.

Children under age 13 years withstanding, Rhode Island mo-

torists still remain unprotected by a mandatory seat belt use law, a fact which places Rhode Island in a shrinking minority of states. By means of data gathered as part of this research, the State has been serving as an external control in an epidemiologic evaluation of the New York State seat belt use law. Preliminary evidence suggests that the law has been effective in reducing injury mortality and morbidity on New York roads, and by implication that Rhode Island has an excess road toll that is attributable to the absence of a law.^{10, 18} The results of the current study highlight sub-groups in the State population, most particularly those in the 15-34 age group, which could be expected to benefit markedly from enactment of seat belt and helmet use legislation.

... Rhode Island motorists still remain unprotected by a mandatory seat belt use law, a fact which places Rhode Island in a shrinking minority of states.

This research has uncovered gross deficiencies in Rhode Island hospital-based data on motor vehicular trauma that need to be remedied in the interests of enhancing documentation, etiology, intervention, evaluation and prevention. In particular, emergency department personnel should routinely collect patient data on restraint and helmet use, as well as on ingestion of alcohol and other drugs. Finally, if E-coding were to be mandated for hospitals, as has already occurred in a few states, this would prove invaluable in systematically addressing both vehicular and non-vehicular trauma in Rhode Island.

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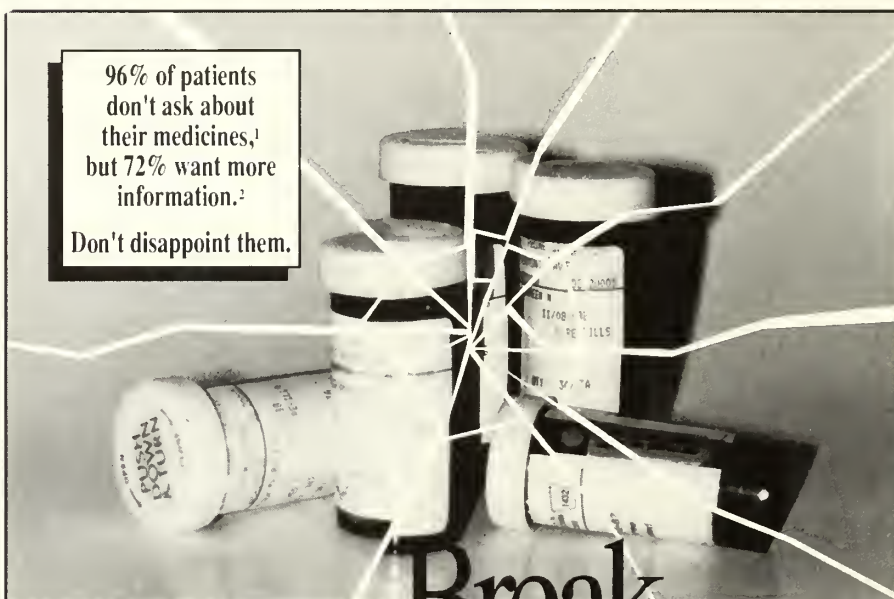
mel Doyle for her role as a medical records technician; Susan Wilkinson for conducting data validation; Eleanor Alger, Brenda Doyle and Maureen Sullivan for contributions to the fieldwork; John Migotsky and Bill Brinson for technical assistance; Dr David Parker for editorial suggestions; Roberta Chevoya and Edward Martin for providing access to the vital records; and to the medical, administrative, and clerical staffs of all participating hospitals. This research was supported by the National Highway Traffic Safety Administration of the US Department of Transportation (Grant DTNH22-91-C05026).

References

- ¹ Campbell M. Rhode Island's Health 1988. Providence RI: Rhode Island Department of Health, 1989.
- ² National Center for Health Statistics. Advance report of final mortality statistics, 1987. Monthly Vital Statistics Report 38, 5 supp., 1989.
- ³ Rockett IRH. Program perspective on injury surveillance: Rhode Island's experience. Public Health Rep 100:591-593, 1985.
- ⁴ Barancik JI, Chatterjee BF, Greene-Craden YC, et al. Motor vehicle trauma in Northeastern Ohio. I. Incidence and outcome by age, sex, and road-use category. Am J Epidemiol 123:846-861, 1986.
- ⁵ Rockett IRH, Lieberman ES, Hollinshead WH, Putnam SL, Thode HC. Age, sex, and road-use patterns of motor vehicular trauma in Rhode Island: A population-based hospital emergency department study. Am J Public Health (in press).
- ⁶ International Classification of Diseases, 9th revision, Clinical Modification. Ann Arbor, MI: Commission on Professional and Hospital Activities, 1978.
- ⁷ US Department of Commerce. 1980 Census of Population. General Population Characteristics, Rhode Island. Washington DC: Government Printing Office, 1981.
- ⁸ Statewide Planning Program. Monthly Progress Report for October 1986. Providence RI: Rhode Island Department of Administration, 1986.
- ⁹ Rockett I, Hollinshead WH, Lieberman E. A statewide motor vehicle injury surveillance system. RI Med J 69:67-70, 1986.
- ¹⁰ Rockett IRH, Hollinshead WH, Lieberman ES. A preliminary assessment of change in motor vehicle trauma incidence and outcome: Rhode Island, 1984-1985. Bull NY Acad Med 64:750-756, 1988.
- ¹¹ Statewide Health Coordinating Council. Rhode Island Health Plan, 1987-1992. Providence RI: Rhode Island Department of Health, 1986.

- ¹² Mechanic D. Sex, illness, illness behavior, and the use of health services. J Human Stress 2:29-40, 1976.
- ¹³ Mechanic D. The influence of mothers on their children's health attitudes and behavior. Pediatrics 33:444-453, 1964.
- ¹⁴ Lewis CE, Lewis MA. The potential impact of sexual equality on health. N Engl J Med 297:863-869, 1977.
- ¹⁵ Magnusson G, Aurelius G. Illness behavior and nationality: A study of hospital care utilization by immigrants and natives in a Stockholm district. Soc Sci & Med 14A:357-362, 1980.
- ¹⁶ Kleinman JC, Gold M, Makuc D. Use of ambulatory medical care by the poor: Another look at equity. Med Care 19:1011-1029, 1981.
- ¹⁷ David K, Rowland D. Uninsured and underserved: Inequities in health care in the United States. Milbank Q 61:149-176, 1983.
- ¹⁸ Barancik JI, Kramer CF, Rhode HC, Harris D. Efficacy of the New York State seat belt law: Preliminary assessment of occurrence and severity. Bull NY Acad Med 64:742-749, 1988.

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Addressing the Health Needs of Mothers and Children in Rhode Island

William H. Hollinshead, MD, MPH
Jane F. Griffin, MPH
Tricia Leddy, MS

This report describes six serious primary maternal and child health problems, along with program opportunities to address these unmet needs.

The Division of Family Health in the Rhode Island Department of Health through its annual needs assessment process has identified six major unmet health needs for mothers and children in the state. Although there are many other important health problems for young families, these six are the highest priority for Division programs and activities. It is important to note that these are pri-

mary health care needs and do not specifically address the needs of children with disabilities or other chronic conditions. This report describes the unmet needs and explains how the Office of Primary Care in the Division of Family Health will address each area of need. The six top priority primary health care needs discussed in this article are:

1. Unintended Pregnancy
2. Perinatal Substance Abuse
3. Late Entry into Prenatal Care
4. Lead Poisoning
5. Immunization
6. Childhood Injury

The newly established Office of Primary Care in the Division of Family Health has made these unmet needs a major focus of its workplan for the coming year.

Unintended Pregnancy

The fertility rate — the number of births per 1,000 women of childbearing age — is important in predicting the size and composition of future Rhode Island families. In Rhode Island during the 1980s, 68% of reported pregnancies resulted in live births, 28% in induced abortions, and 4% in spontaneous abortions ("miscar-

riages"). Figure 1 shows the changes in fertility and induced abortion rates since 1973.

Currently, the average fertility rate in Rhode Island is 57 births per 1,000 women while in the United States it is 67 births per 1,000 women. This difference has been consistent over the past fifteen years. There has been little fluctuation in the Rhode Island and United States fertility rates from 1973-1987. However, induced abortion rates rose, both in the United States and Rhode Island, during the 1970s, and then levelled off in the 1980s. This rise in induced abortions accounts for the increase in the overall pregnancy rate, even though the fertility rate did not change.

Both the number of pregnancies and the number of women of childbearing age increased during the 1980s.¹ Therefore, the absolute number of pregnant women requiring services has increased. In 1980 there were 18,184 reported pregnancies in Rhode

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ABBREVIATION USED:
CPSP: Comprehensive
Prenatal Service Program

Island, with 12,166 births. In 1987 there were 20,472 pregnancies, with 14,041 births reported to the Department of Health.

Unintended pregnancy has far reaching effects on the mother, father, child, family and community. Although unintended pregnancies are costly at all levels, the burden weighs most heavily on three groups least able to bear the cost: black women, women in lower socio-economic groups, and teenage women.

Teenagers who experience an unintended pregnancy are the most vulnerable group. In Rhode Island 50% of the pregnancies to teenagers aged 14-18 end in induced abortion, whereas only 27% of the pregnancies to women over 18 end in induced abortion (Figure 2).

Since teenagers have a much higher percentage of pregnancies ending in induced abortion than older women, the need for family planning services to teens is most critical.

Induced abortions are markers of unwanted pregnancy and indicate a need for family planning services. Since teenagers have a much higher percentage of pregnancies ending in induced abortion than older women, the need for family planning services to teens is most critical.

Several new and existing programs in the Office of Primary Care are focused on decreasing unintended pregnancies especially among teens. The federally funded Family Planning Program and the state-funded Family Life Program provide comprehensive family planning services. Services in these programs include physical exam, diagnostic screening tests, education, and distribution

Figure 1. Fertility Rate and Induced Abortion Rate, United States and Rhode Island, 1973-1987.

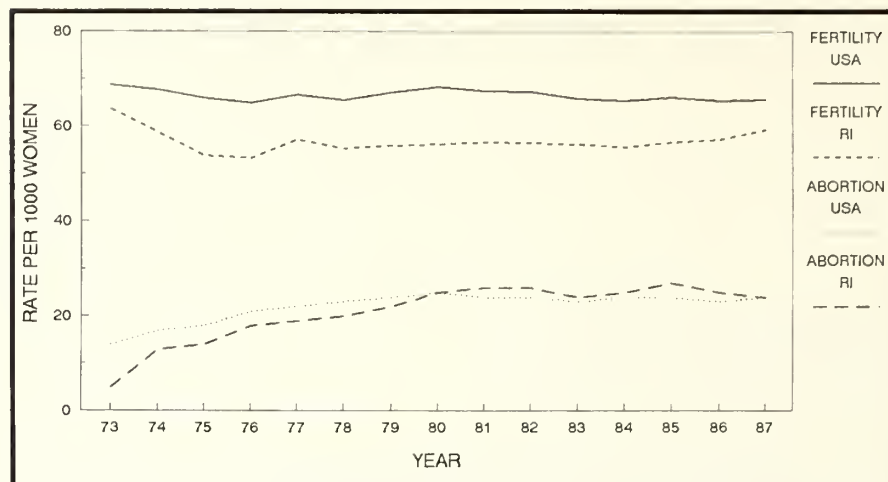
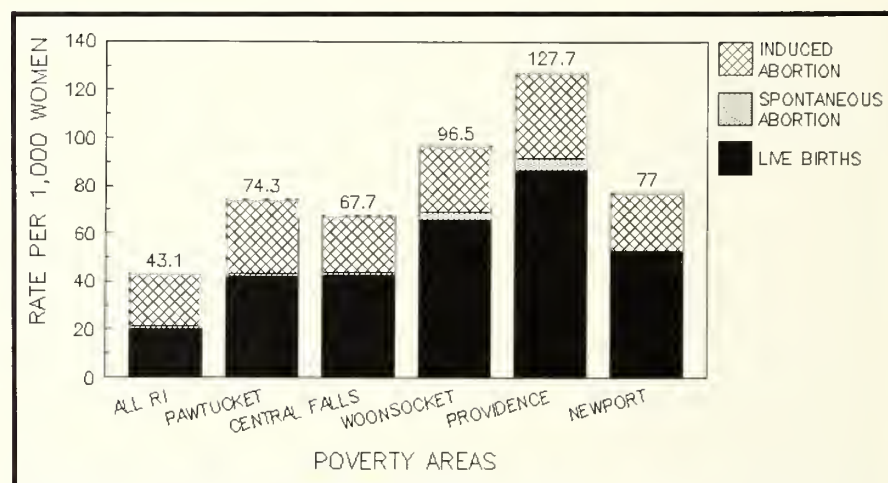


Figure 2. Pregnancy Rates for Women Ages 14-18, Selected Poverty Areas, Rhode Island, 1981-1985 Average.



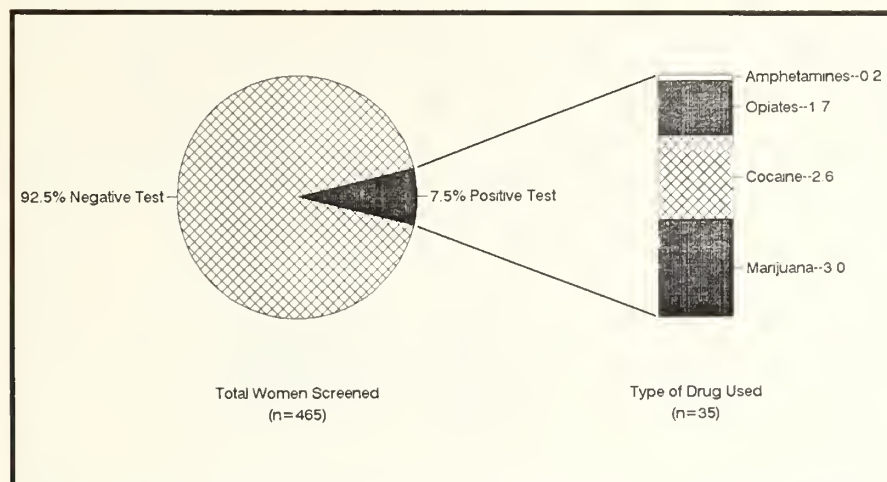
of family planning methods, and are provided through contracts with community health centers, hospital clinics, and visiting nurse agencies. These programs will serve over 14,000 women in the coming year. Twenty-three percent served in 1989 were teenagers, 29% were minorities, and over half were living below poverty level, the rest residing in low-income working families.

In addition to the basic clinical service programs, two Family Life-funded special projects, one in inner city Providence, the second

in Pawtucket and Central Falls, will coordinate sex and family life education in these communities. These projects stress community education programs and network building to increase understanding of teen sexuality and to help parents, peers, physicians and other health care providers respond appropriately to the needs of teenagers in these inner city areas.

The Teen Theatre Troup is a recent project, funded by the federal Family Planning Program. This one-year initiative intended

Figure 3. Perinatal Drug Use in Rhode Island, 1989.



to provide peer education on issues of prevention of unintended pregnancy through theatrical performances by a student drama troupe to middle school students in the city of Providence. This program, run by the Langston Hughes Center for the Arts in Providence, was extremely successful and well-received. This initiative will be funded again this year in order to continue to help adolescents acquire decision-making skills regarding lifestyle issues such as using drugs and alcohol, sexual activities and other risk taking behaviors. There is particular focus on prevention of unintended pregnancy through the dramatization of the changed lifestyle of a single teenage mother.

A new Family Planning initiative is scheduled this year to increase the involvement and responsibility of teen males in teen pregnancy prevention. This program will be designed with the help of young males in inner city Providence, Pawtucket, and Central Falls. The program's goal is to reduce unintended pregnancy and sexually transmitted diseases. This will be achieved by improving male attitudes concerning sexuality and by increas-

ing sexuality education levels and responsible sexual behavior in young men in the target communities.

Furthermore, in order to decrease subsequent unintended pregnancies occurring closely after a birth, protocols will be established and staff training will be completed over the coming year to assure that all pregnant women receiving prenatal care at Rhode Island Department of Health-funded prenatal clinics will receive family planning counseling, and contraception methods if appropriate, in the third trimester and immediately postpartum before hospital discharge.

Perinatal Substance Abuse

Due to reported increases in drug use (especially cocaine) and concern over the severe effects on pregnant women and their newborns, the Department of Health conducted a statewide prevalence study of all maternity patients in the Fall of 1989.² The purpose of this study was to determine the need for drug abuse prevention and treatment service for pregnant women in the state and to provide baseline data to see if the perinatal drug problem changes over time.

Four hundred and sixty-five specimens were collected from all maternity hospitals in the state. The results showed that 7.5% of the patients had used drugs within 48 hours of delivery. Figure 3 shows the types of drugs used by the 35 women who tested positive. Of the positive drug users, 40% used marijuana, 34% used cocaine and 23% used opiates.

Cocaine users are more likely to be living in poverty areas, to already have children, to be non-white, and to be covered by public insurance.

Applying these percentages to 14,000 Rhode Island births in a year gives the following annual projections of drug use in the perinatal period:

Type of Drug	Estimate per year
marijuana users	= 420
cocaine users	= 364
opiate users	= 238

The results from the study showed that women with public insurance (Medical Assistance and Rte Start) are four times more likely to be using illicit drugs than women with private insurance. Cocaine users are more likely to be living in poverty areas, to already have children, to be non-white, and to be covered by public insurance.

The Office of Primary Care will address the problem of perinatal substance abuse by increasing identification of prenatal substance abuse, and by increasing the use of existing substance abuse treatment resources for pregnant women. In order to increase identification of prenatal substance abuse the Office will provide grant support for prenatal social workers at all publicly funded prenatal clinics, located in non-profit community health

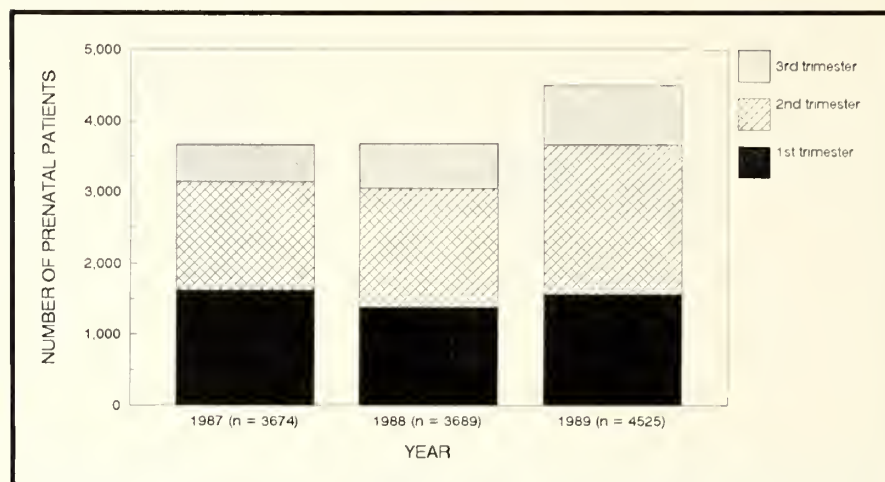
centers and hospitals. The social worker will assess each prenatal patient for psychosocial risks and needs, and will screen for adverse health behaviors, in particular, drug and alcohol abuse. These social workers will receive an interviewing protocol and training on identifying drug or alcohol abuse and appropriate referral. Women identified as substance abusers will receive counseling, and referral to appropriate substance abuse treatment. In addition, treatment will be monitored through the assignment of a case manager in conjunction with ongoing prenatal care.

The Rite Start Program, in the Office of Primary Care, provides maternity care, including substance abuse treatment when appropriate, to uninsured pregnant women who are not eligible for Medical Assistance and have family incomes less than 200% of the poverty level. Rite Start has compiled a resource directory of all substance abuse treatment facilities in Rhode Island which treat pregnant women in order to increase their use among this population where appropriate. Pertinent information, such as whether Medical Assistance and Rite Start are accepted as payment for the services, is included. This resource directory has been distributed to all publicly-funded prenatal clinics, and will soon be distributed to all obstetrical providers in the state.

Late Entry Into Prenatal Care

The Institute of Medicine identified four major barriers to prenatal care in the United States.³ These barriers included 1) financial access (insurance coverage), 2) inadequate system capacity, 3) organization, practices, and atmosphere of prenatal services and 4) cultural and personal barriers. Rhode Island has reduced several

Figure 4. Trimester of First Prenatal Visit Among Women Enrolled in Comprehensive Prenatal Services Program, 1987-1989.



of these barriers through the implementation of the Rite Start Program, and by expansion of Medical Assistance for pregnant women.

Results from the Division of Family Health's Comprehensive Prenatal Service Program (CPSP) show that there are still barriers to care for low income women. CPSP supports prenatal care programs located in 13 community health centers and three hospital outpatient clinics throughout Rhode Island. In 1987 there were 3,674 prenatal patients registered at the CPSP sites; in 1989 this increased to 4,525 patients for a 23.2% increase in two years.

However, on average pregnant women who participate in the CPSP program have been entering prenatal care later. Figure 4 shows the decline in first trimester enrollment. In 1987 44% of the CPSP patients enrolled for care in the first trimester while in 1989 first trimester enrollment dropped to 34.5%.

This trend is indicative of a prenatal care system that is struggling to meet the needs of its patients. There are still many low-income women without coverage for maternity care in early preg-

nancy. Waiting times are too long at some sites. In addition, CPSP sites report that recruiting, retaining and supporting professionals to staff their prenatal clinics is an ongoing problem.

Early and continuous prenatal care is associated with better pregnancy outcome and is critical for prevention of low birth weight and other complications.

Clearly there are many low income maternity patients who need earlier prenatal care. Early and continuous prenatal care is associated with better pregnancy outcome and is critical for prevention of low birth weight and other complications. Rhode Island has entitled all low income women to maternity care coverage through Medical Assistance and Rite Start, but there are still serious delays in both coverage and care. Now Rhode Island must build its capacity to ensure early prenatal coverage and care for all women.

Before the Office of Primary Care can develop and implement a plan to address the growing problem of late onset of prenatal

Table 1. Childhood Lead Poisoning Screening Volume and Yield by Provider, 1977-1989

Year	PUBLIC PROVIDER			PRIVATE PHYSICIAN			ALL PROVIDERS		
	Number Screened	Number Positive	Percent Positive	Number Screened	Number Positive	Percent Positive	Number Screened	Number Positive	Percent Positive
1977	5,386	437	8.1	658	18	2.7	6,044	455	7.5
1978	4,157	356	8.6	1,448	36	2.5	5,605	392	7.0
1979	6,310	496	7.9	1,727	58	3.4	8,037	554	6.9
1980	7,418	326	4.4	1,993	36	1.8	9,411	362	3.8
1981	7,010	176	2.5	3,166	50	1.6	10,176	226	2.2
1982	7,546	378	5.0	2,686	50	1.8	10,232	428	4.1
1983	7,489	333	4.4	2,873	71	2.4	10,362	404	3.8
1984	9,628	325	3.4	2,790	44	1.6	12,418	369	3.0
1985	11,527	231	2.0	3,113	49	1.5	14,640	280	1.9
1986	10,345	176	1.7	4,877	47	0.9	15,222	223	1.4
1987 ¹	10,700	331	3.0	6,755	96	1.0	17,455	427	2.0
1988	10,858	510	4.6	7,665 ²	118	1.5	18,523 ³	628	3.0
1989	11,480	530	4.6	9,151	159	1.7	20,631	689	3.3
TOTAL	109,854	4,605	4.1	48,902	832	1.7	158,756	5,537	3.4

¹ Program adopted CDC guidelines for positive cases of Ep>35 micrograms/dl and Pb>25 micrograms/dl — 6/30/87 (Ep = Erythrocyte Protoporphyrin)

² HMOs and some door-to-door screenings are counted under Private Physician rather than Public Provider

³ There were 21,762 screening events however, 3,239 were children over six years of age, adults and other non-classified specimens

care in publicly-funded prenatal clinics, a clearer definition of the problem is needed. Why are women coming later for prenatal care? Are pregnant women calling for appointments later, is the waiting time for an initial prenatal visit longer due to an overwhelmed system, or are there other explanations for late entrance into prenatal care in publicly-funded clinics? The Office of Primary Care and the Office of Data and Evaluation will conduct an assessment over the next six months, in conjunction with publicly-funded prenatal care agencies, to identify any barriers to early prenatal care, and will develop and implement a plan to eliminate barriers and increase first trimester prenatal care.

Childhood Lead Exposure

The Division of Family Health recognizes exposure to lead as the state's most important children's environmental health hazard. The Childhood Lead Screening Program works with an extensive net-

work of Rhode Island providers to screen children for elevated blood lead levels. In addition, the program provides door-to-door screening in high-risk neighborhoods. In 1989, the program and its referral network screened over 21,000 children, and detected 716 cases with elevated blood lead levels. This represents a continuing increase in the numbers of children screened and detected annually. Table 1 shows this increase.

However, there are two very significant limitations to programs which rely solely on screening and case-finding (ie, secondary prevention strategies) for addressing the hazards of environmental lead exposures:

1. Substantial numbers of children with elevated lead levels will continue to go unscreened and undetected, because they do not have regular providers of pediatric care.
2. The current screening tests do not reliably detect lower

blood lead levels known to be associated with certain types or irreversible toxicity.

A secondary prevention strategy is a very effective mechanism for preventing the harmful effects of untreated overt lead poisoning, with such complications as permanent mental retardation, severe encephalopathy, and death. However, it cannot prevent the more subtle and insidious effects of lower level lead toxicity that can significantly impair the health and educational performance of large numbers of children. Addressing these latter effects requires a primary prevention strategy that emphasizes risk assessment and risk reduction.

The Office of Primary Care provides funding to community health centers and hospitals to provide primary pediatric care to children under age six. Most of these children are living in poverty or near poverty; many have no health insurance. Health Department funds ensure that there are no financial barriers to pre-

ventive pediatric care for these children; families are charged on a "sliding fee scale," based on their ability to pay.

The Office of Primary Care will ensure over the coming year that Department of Health-funded pediatric care agencies will routinely provide both primary and secondary lead poisoning prevention activities.

Substantial numbers of children with elevated lead levels will continue to go unscreened and undetected, because they do not have regular providers of pediatric care.

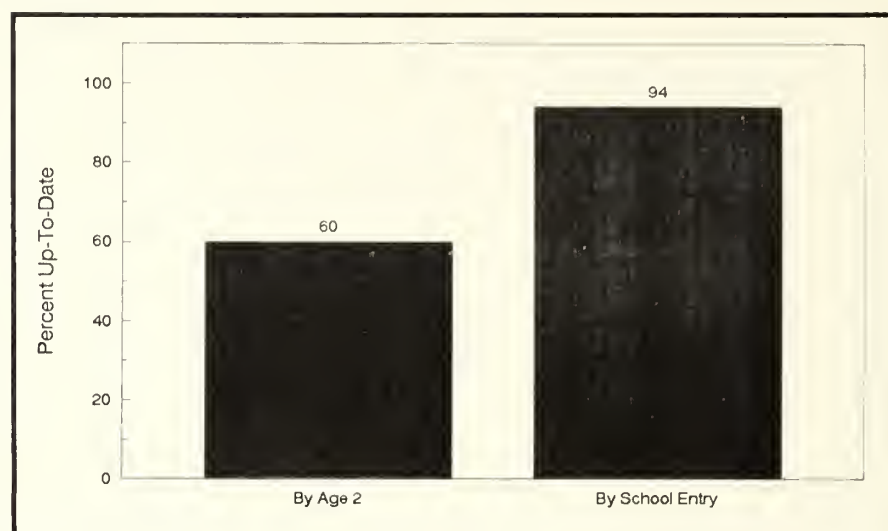
Primary prevention activities will include prevention education strategies targeted to parents and caretakers of preschool children. The Office will develop lead poisoning education protocols to be incorporated into routine pediatric care, and will provide training to pediatric providers on providing parents lead poisoning prevention education. The training will include an update on known sources of lead exposure in children.

The Office will also address secondary prevention by providing training with lead screening protocols for Department of Health-funded primary pediatric care agency staff. This training will include blood collection techniques, risks and effects of lead exposure, interpretation of results, and appropriate follow-up and treatment. Protocol updates and training programs for agency pediatric staff will be conducted in conjunction with the Childhood Lead Screening Program.

Immunization Compliance

Rhode Island's "overall" immunization rate for children is very good. In the 1988-89 school year,

Figure 5. Percent of Children with Up-To-Date Immunizations (n = 1789), Rhode Island, 1989.



97.7% of all students entering kindergarten were adequately immunized. Public school students were somewhat lower at 94.5% and transfer students had the lowest rate of immunization compliance — 93.0%. However, in a retrospective study of 1,789 students entering kindergarten in 1989 it was found that only 60% were adequately immunized at their second birthday (Figure 5). All pediatric sites need to monitor immunization compliance to ensure that their two year old patients are adequately immunized.

Over the coming year, the Office of Primary Care will work in conjunction with the Department of Health Immunization Program and funded primary pediatric care agencies to improve childhood immunization rates at age two and to assure that all children are adequately immunized by the first day of school. This will be accomplished through assuring that all pediatric agencies have a working system to identify and vaccinate all patients who are out of compliance with the recommended immunization schedule. The Office of Primary Care, in conjunction with the Immuniza-

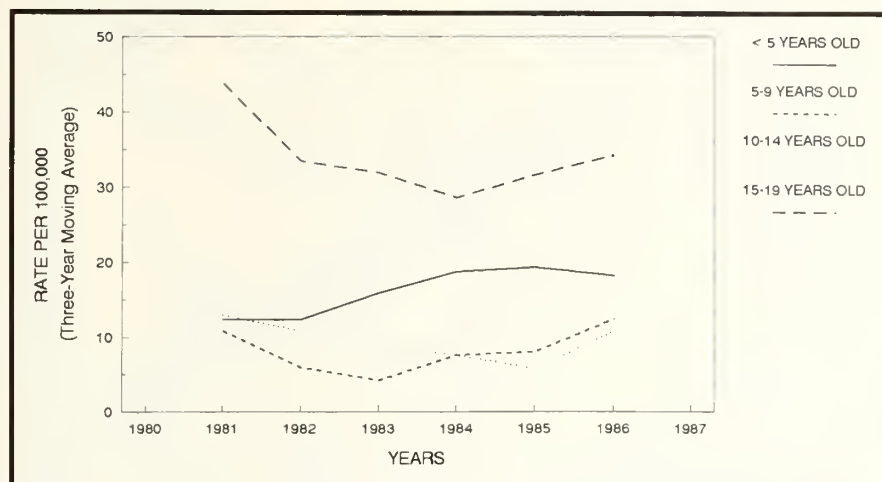
tion Program, will provide training and technical assistance to agencies on this immunization tracking system. In addition, all pediatric agencies are being required to develop a system to provide prompt vaccination on an emergency basis, such as for school entry.

Injury

Injuries remain the leading cause of death and hospitalization for children over the age of one in the United States.⁴ The vast majority of injuries to children are preventable. Figure 6 shows Rhode Island's injury death rates for age-specific groups of children and adolescents less than 20 years old. These rates are three year averages that show the trend throughout the 1980s. Teenagers aged 15-19 years old consistently have the highest death rates. The majority of these deaths are to males and are due to motor vehicle crashes.

The group with the next highest injury death rate is children less than 5 years old. The injury rate in this group has been on the rise during the 1980s. The actual numbers are small, which causes

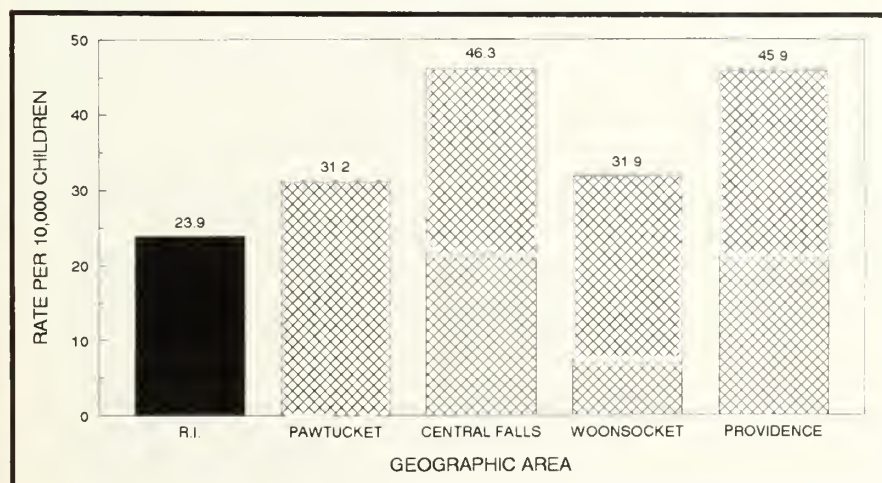
Figure 6. Injury Mortality Rate, Ages 0-19 Years Rhode Island, 1980-1987.



sources for these low-income families to modify their home environment. Rhode Island has recently received support for a major injury control initiative. With wide community participation, the Department is leading efforts to reduce auto injuries, violence, and other preventable trauma with a special focus on young children and adolescents.

Rhode Island has recently received support for a major injury control initiative.

Figure 7. Pediatric Injury Hospital Rates, Children Aged 0-4, Rhode Island, 1981-1985.



wide fluctuations from year to year. However, the three year average in Figure 6 shows a distinct and worrisome trend, which seems to be continuing.

In Rhode Island, approximately ten young children under five years of age die each year from preventable injuries, including burns, poisonings, and trauma. In addition, there are, on average, 136 children under age five hospitalized overnight each year for serious preventable injuries. Figure 7 shows the rate of hospitalization for pediatric injuries in se-

lected Rhode Island cities. Central Falls, Providence, Woonsocket and Pawtucket have the highest rates of hospitalizations for pediatric injuries in the state. Both Central Falls and Providence have a rate of preventable childhood injury that is twice the state average of 23.9 per 10,000. These cities have the most concentrated areas of poverty in the state, and children from poorer families have higher injury rates.

Injury prevention programs must focus not only on safety education, but also on providing re-

The Office of Primary Care will ensure that infant and childhood injury prevention is an integral component of prenatal and primary pediatric care at Department of Health-funded prenatal and pediatric care agencies. The Office will develop updated protocols for and provide training to prenatal and pediatric staff at these agencies on integration of infant and childhood injury prevention education into last trimester of prenatal care, into the perinatal hospital discharge protocol, and into routine pediatric care. The Office of Primary Care will provide parent education materials on childhood injury prevention, including videotapes for the waiting room and written materials to reinforce education provided on such subjects as correct use of car seats, the importance of home smoke detectors, child proofing the home, and how parents can get help and support for overwhelming problems and stresses that if ignored can result in child abuse. Training for pediatric care providers will focus on the main causes of childhood injury and death, including how to identify parents at risk for child abuse and provide appropriate problem solving resources and support, how to identify and report suspected child abuse, the

correct use of approved car seats, the most critical parts of home child-proofing, and the landlords' responsibility under current law in the area of tenant safety including smoke alarms, lead paint removal and other critical items.

Mothers and children in Rhode Island have many health care needs. This report describes six serious primary maternal and child health problems, along with program opportunities to address these unmet needs. It is not an exhaustive list, but rather a selection among top priority needs that will do the most to improve the health of the youngest and most vulnerable citizens of Rhode Island.

References

- ¹ Ventura, S., et al. "Estimates of Pregnancies and Pregnancy Rates for the United States 1976-85" American Journal of Public Health 78(5), 1988.
- ² Centers for Diseases Control, "Statewide Prevalence of Illicit Drug Use by Pregnant Women — Rhode Island," Morbidity and Mortality Weekly Report 39(14), 1990.
- ³ Institute of Medicine, *Prenatal Care: Reaching Mothers, Reaching Infants*, National Academy Press, Washington, DC 1988.
- ⁴ Office of Technology Assessment, *Healthy Children: Investing in the Future*, Washington, DC 1988.

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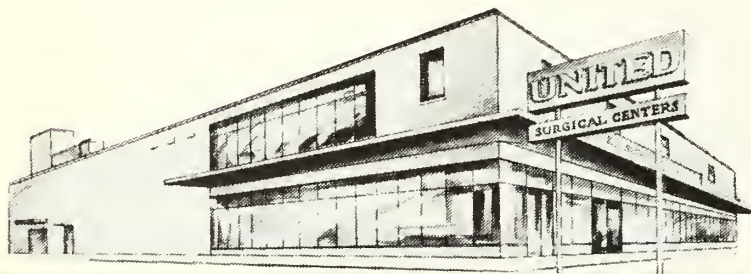
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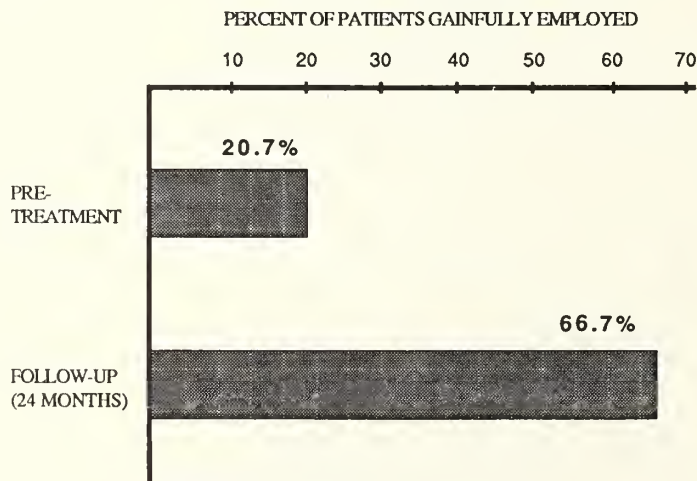
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A Case of Tuberculoid Leprosy in Rhode Island

Ellen H. Frankel, MD
Betty P. Teng

With the influx of people entering the United States from India, southeast Asia and Central Africa, it is likely that future cases of leprosy will appear in Rhode Island.

Leprosy is a chronic disease caused by the acid-fast obligate intracellular mycobacterium, *Mycobacterium Leprae*. Affecting primarily the peripheral nervous system and the skin, leprosy, or Hansen's Disease (HD), is infectious, though the degree of its infectiousness varies with the different forms the disease may take. Persons of any age can contract leprosy, although children are more susceptible because they have weaker immune systems and customarily spend more time in close contact with adults who may have HD.

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Betty P. Teng is a preceptor of Dr Frankel, Yale University.

Transmission of *M. leprae* bacilli can occur in a number of ways: through the skin, the mucous membranes, and sometimes the gastrointestinal tract. Persons may become infected by way of skin-to-skin contact; by aerosol through nasal mucosa; through ingesting food infected by flies carrying the bacilli; and babies may contract the disease through taking their infected mother's milk. For all these reasons, people living in poor, overcrowded areas endemic for leprosy are more likely to develop the disease. Thus, incidence of HD is highest in the developing countries of Central Africa and Southeast Asia, as well as India. Though leprosy is less common in the colder regions of the globe, in the US, doctors have diagnosed cases of the disease in California, Hawaii, Louisiana, New York City, and Texas.

Yet, as mentioned before, the degree to which HD is infectious varies with its different forms.

There are polar forms of the disease, classified as **Tuberculoid (TT)** leprosy and **Lepromatous (LL)** leprosy, with intermediate forms having a great variety of manifestations in between what form of HD develops in a patient depends on the level of resistance a host lodges against the *M. leprae* bacilli. TT results when there is a high level of host response,² while LL develops when there is no such resistance. Thus, TT cases are usually termed non-infectious or "closed," while cases of LL are infectious, or "open."³

In histological examinations of tissue taken from TT patients, AFB (acid-fast bacilli) are often absent, while bacilli are abundant

ABBREVIATIONS USED:

AFB: acid fast bacilli

HD: Hansen's disease

LL: lepromatous leprosy

SPF: sun protection factor

TT: tuberculoid leprosy

in the skin lesions of LL patients. As a result, LL patients are more apt to be contagious, while it is more difficult for persons with TT leprosy to infect others. Lepromatous leprosy is also called the multibacillary form of the disease while tuberculoid leprosy is the paucibacillary form of HD.

This is not to say, however, that persons with tuberculoid leprosy are not harmed by the disease. Just as TT and LL result from different host reactions to *M. leprae* infection, tuberculoid and lepromatous leprosy have different effects on the body. While TT does more damage to the nerves, LL affects primarily the skin. Both are commonly manifested by lesions appearing on the skin, but in tuberculoid cases, lesions are well-defined, flat, hypopigmented and somewhat anaesthetic. They occur in exposed, isolated areas of the body, appearing singularly or in pairs, and seldom exceed three in number. At these isolated areas, nerve damage will be greatest, thus the loss of feeling in the lesions. In lepromatous cases, skin lesions are not well-defined, vaguely hypopigmented, and nodulated, and they are wide-spread and symmetrical. Though the nerves of patients with lepromatous leprosy will also suffer nerve damage, loss of nerve function occurs much more slowly than in patients with tuberculoid leprosy. With the paucibacillary disease, however, there is a tendency to spontaneous regression and TT requires a much shorter time of treatment than the multibacillary disease, where there is more of a possibility of a relapse and/or the development of drug resistance.

There are also borderline cases of HD, in which patients experience the complications of both the tuberculoid and the lepromatous forms of the infection. Those tending to have more tuberculoid qualities than lepro-

matous are classified as borderline tuberculoid (BT) cases, while patients with an infection more similar to lepromatous leprosy are classified as borderline lepromatous (BL) cases. Such patients are treated with a combination of methods used to treat tuberculoid leprosy and lepromatous leprosy.

Case Study

A 3 and 1/2-year-old girl first came to our office on November 20, 1989 because of a 0.6 cm non-healing lesion on her right cheek, present for 6 months. Physical examination showed that she had an atrophic, hypopigmented, and slightly anaesthetic macule on her face. She had been previously treated with a topical cortisone product, which gave some relief, but her parents stated that stopping use of the cream had caused the lesion to flare again. Discoid lupus erythematosus was initially diagnosed, with leprosy in the differential diagnosis. A week later the patient returned and was given a sunscreen with SPF 50 to use daily, along with a twice daily application of Vytone 1% cream (hydrocortisone 1%/iodoquinol 1%). Two weeks after her first visit, the lesion was still unchanged, prompting a suspicion of leprosy. On December 11, 1989, a 3mm punch biopsy of the lesion was taken and sent for pathologic analysis. The tissue was negative for AFB pathological organisms yet revealed a non-caseating granulomatous inflammation of the superficial and deep dermis, with an associated dense lymphoplasmicytic infiltrate. The pathologist suggested lupus vulgaris, mycobacterial infection or tuberculoid leprosy as possible diagnoses.

Our patient is an Indian girl who came to Rhode Island in July, 1989 for adoption by American parents. She was born and raised in

Pune, India, an area endemic for leprosy. With this information in mind, we asked that the biopsy sections be sent to the Gillis W. Long Hansen's Disease Center in Carville, Louisiana for further pathologic study. In late February, 1990, we received a confirmation from Carville that our patient did indeed have tuberculoid leprosy. A fluctant pustule, approximately 4mm in diameter was noticed on her right lower quadrant. A daily dosage of 25mg of dapsone along with 150mg of rifampin was immediately prescribed.

One month later, with medication, the abdominal lesion had disappeared and the facial lesion had resolved to a hypopigmented macule. Eight weeks after starting the dapsone/rifampin treatment, we found that she had continued to improve, yet brown macules had appeared on her right palm and right foot. In June, after 14 weeks of treatment, the lesion on her cheek had resolved to a faint hypopigmented macule on her face. All other lesions had completely resolved.

Discussion

Like many TT patients, our patient had a single, well-defined macule and her biopsy showed no signs of AFB. In children, TT is the predominant form that leprosy takes.⁴ Seldom do children contract the LL form of the disease. Clinically, our patient's case was also typical of the way leprosy manifests itself in children. According to Sehgal and Srivastava, "In a vast majority of children, the lesion is usually a solitary one." They also state that the "majority of children are shown to suffer from indeterminate and tuberculoid leprosy."⁵

As seen with our case presentation, multidrug treatment is most effective in the treatment of Hansen's Disease. The World

Health Organization recommends dapson, rifampin and clofazimine as the best medications for combating the disease.

Comment

For help and information on the treatment of HD, the Gillis W. Long Hansen's Disease Center in Carville, Louisiana is the national HD control center in the United States. Nearly all of the estimated 5000 leprosy patients in the US are outpatients of the Carville Center.⁶ It also serves as the headquarters for regional HD centers operating in Boston, Chicago, Los Angeles, Miami, New York, San Diego, San Francisco, Seattle, Texas, Puerto Rico and Rhode Island. In RI, the author now serves as the state's regional representative to the national Hansen's Disease center in Carville.

With the influx of people entering the US from India, south-east Asia and Central Africa, it is likely that future cases of leprosy will appear in Rhode Island.

Acknowledgement

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References

- ¹ Pfaltzgraff, Roy E., *How to Diagnose and Classify Leprosy: A Study Guide*, American Leprosy Missions, Elmwood Park, NJ, 1988, pg. 22.
- ² Ibid.

⁴ Arnold, Harry L. Jr., *Modern Concepts of Leprosy*, Charles C. Thomas Publishing, Springfield, IL., 1953, pg. 22.

⁵ Sehgal, Vivender N., Srivastara, Govind, "Leprosy in Children," *International Journal of Dermatology*, Vol. 26, No. 9, pp. 557-566, Sept. 1987.

⁶ Ibid.

⁶ Ahmann, Sarali, "Braving the Ancient Stigma of Hansen's Disease," *Skin and Allergy News*, Vol. 21, No. 6, pp. 1, 32, June 1990.

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Management of Postpartum Uterine Atony

Roger J. Ferland, MD
Lisa M. Adler, MD

Atony should be suspected when excessive blood loss is noted during the immediate post-partum period.

Uterine atony, the failure of myometrial contraction after delivery, accounts for most cases of postpartum hemorrhage and is the leading cause of maternal death in the United States. The most important mechanism responsible for hemostasis at the placental bed after delivery is uterine contraction and subsequent tamponade of vessels supplying the implantation site. Failure of adequate uterine tone following delivery can cause rapid hypovolemic shock which may become irreversible if not recognized and treated promptly.

Conditions commonly associated with uterine atony include retained secundines, chorioam-

nionitis, and grand multiparity. Other risk factors are uterine overdistention from multiple gestation or hydramnios, uterine leiomyomata, tocolytic therapy near the time of delivery, and general anesthesia with halogenated compounds. Atony has been recently described following malignant hypothermia prophylaxis with dantrolene (Dantrium®).¹ In this case, the patient developed uterine atony following primary cesarian section for which she had received 200 mg of dantrolene intravenously. Efforts at pharmacologic treatment failed and the patient required hysterectomy to control hemorrhage. Dantrolene is known to cause relaxation of skeletal, cardiac, and gastrointestinal smooth muscle, and may decrease oxytocin induced contraction of the myometrium.

Atony should be suspected when excessive blood loss is noted during the immediate postpartum period. The diagnosis is confirmed by palpating a soft, poorly contracted uterus. The clinician must rule out retained products of conception, lacerations, coagulopathy, and uterine inversion. Uterine massage by bimanual compression will often

provoke adequate uterine contraction at least for a short time. A more sustained contraction may require pharmacologic agents (Figure 1). Management should begin with resuscitative measures for rapid loss of blood volume: large bore intravenous access and adequate crystalloids to maintain hemodynamic stability. Addition of plasma expanders, packed red blood cells and fresh frozen plasma may be necessary. With continued bleeding, blood should be drawn to assess hemoglobin and hematocrit, electrolytes, calcium, coagulation parameters, and arterial blood gases. Oxygen therapy should be initiated and an airway maintained. A foley catheter should be placed to monitor urine output.

Intravenous oxytocin, (Pitocin®, Syntocinon®) ten units intravenous push and 20-50 mu/min infusion is appropriate first line therapy to alleviate uterine atony. Oxytocin has a relaxing effect on vascular smooth muscle, and blood pressure may fall as peripheral resistance drops transiently. Although this effect may be pronounced during spinal anesthesia or sympathetic blockade, the drop in blood pressure is typically followed by a small

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sustained rise and does not usually complicate resuscitative measures. Oxytocin may fail to contract a "tired uterus" which has had its receptors saturated by induction or augmentation of labor.

Ergonovine (Ergotrate®) and methylergonovine (Methergine®) are well known stimulators of myometrial contraction and are generally considered second line therapy to oxytocin because of their effects on the peripheral vasculature. Peripheral vasoconstriction can occur causing a hypertensive response and decreased perfusion, aggravating the lactic acidosis which often accompanies hypovolemic shock. Capillary endothelial injury leading to microangiopathic thrombocytopenia and hemolysis may also occur. For these reasons, the ergot alkaloids are relatively contraindicated among patients who develop pregnancy induced hypertension.

Failing effective restoration of uterine tone by oxytocin and ergonovine, prostaglandins have proven useful. Dinoprostone (Prostin E2®) vaginally or intravenously, and dinoprost tromethamine (Prostin F2 alpha®) intramuscular or intramyometrial have been demonstrated by several authors to reverse uterine atony.²⁻⁵ Prostin F2 alpha® is reported to be successful in 87% of cases. Intramyometrial injection appears more effective than intramuscular injection because the decrease in peripheral perfusion in hypotensive patients may interfere with systemic absorption. The usual dose is 1 mg intramyometrially. This can be repeated in five minutes if an adequate response is not achieved with the initial dose. If prompt resolution does not occur, chorioamnionitis is common among cases of treatment failure and may have a causal relationship.^{4,6} Adverse re-

actions secondary to prostaglandins' effect on gastrointestinal and vascular smooth muscle include nausea, vomiting and diarrhea, and changes in blood pressure. A recent case report suggests a significant intrapulmonary shunt up to 28.4% causes transient decreases in oxygen saturation, with a mean decrease of 10.4%.⁷ The author suggests monitoring with a pulse oximeter and appropriate ventilatory support until oxygen saturation stabilizes when using prostaglandins.

Finally, patients who fail to respond to massage and pharmacologic measures are best treated with hypogastric artery ligation or hysterectomy. Aggressive and timely supportive, medical, and surgical therapy are essential elements in treating this common cause of postpartum hemorrhage.

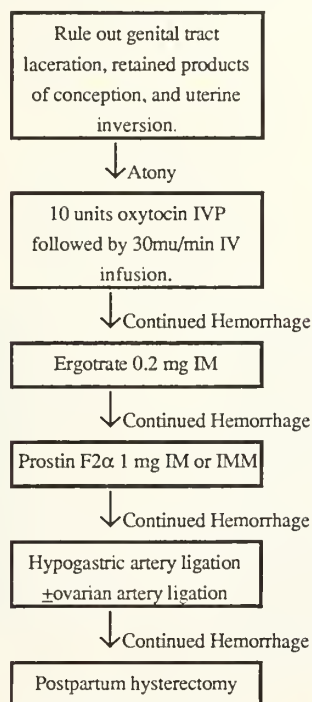
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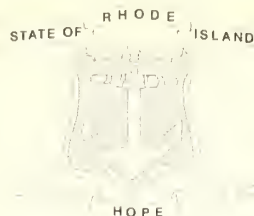
- 1 Weingarten AE, Korsh JI, Newman GG, Stern SB. Postpartum uterine atony after intravenous dantrolene. *Anes Analog* March 1987;66:269-70.
- 2 Bruce SL, Paul RH, Van Dorsten JP. Control of postpartum uterine atony by intramyometrial prostaglandin. *Obstet Gynecol* June 1982;59:549-50.
- 3 Hayashi RH, Castillo MS, Noah ML. Management of severe postpartum hemorrhage with a prostaglandin F-2-alpha analogue. *Obstet Gynecol* June 1984;63:806.
- 4 Theiry M. Control of persistent primary postpartum hemorrhage due to uterine atony with I.V. PGF-2-alpha. *Br J Obstet Gynecol* Oct 1983;90:988.
- 5 Hertz RH, Sokol RJ, Dierker LJ. Treatment of postpartum uterine atony with PGF-2-alpha vaginal suppositories. *Obstet Gynecol* July 1980;56:129-30.
- 6 Takagi S et al. The effects of intramyometrial injection of PGF-2-alpha on severe postpartum hemorrhage. *Prostaglandins* 1976; 12:565.
- 7 Hankins GD, Berryman GK, Scott RT, Hood D. Maternal arterial desaturation with 15-methyl prostaglandin F-2-alpha for uterine atony. *Obstet Gynecol* Sept 1988;72:367-70.

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Figure 1.

POSTPARTUM HEMORRHAGE





HEALTH BY NUMBERS

Rhode Island
Department of Health
H. Denman Scott, MD, MPH
Director of Health

Decline in Smoking-Related Mortality among Rhode Island Physicians

Declines in smoking in the United States have contributed to reduction in heart disease, stroke, and lung cancer, among some populations. In Rhode Island, where prevalence of smoking by physicians has been monitored since 1963, the proportion of white male physicians aged 25 years or older who smoked declined by 73% from 1963 to 1983 (Table 1). To examine the health effects of reductions in smoking, mortality trends among white male physicians and other white males in Rhode Island have been examined using the State's vital statistics. (Non-white and female physicians were excluded because there were too few deaths in these categories to analyze.)

For 1968-1987, death certificate information for deaths of resident Rhode Island white men aged 25 years or older was grouped by the following cause-of-death categories: all causes, smoking-related cancers (oral, larynx, pharynx, esophagus, trachea, bronchus, lung, pancreas, and bladder), and heart disease and stroke. Definitions from the 1970 US Census were used to group deaths by two occupational categories — physicians, and all others.

Census data from 1970 and 1980 were used to estimate the populations of physicians and nonphysicians. Age-standardized mortality rates were calculated for persons 25-64 years of age to ensure compatibility between the

Table 1: Percentage of white men ages 25 years and over who smoke cigarettes, by physician/nonphysician, Rhode Island and United States, circa 1965, 1975, 1985.

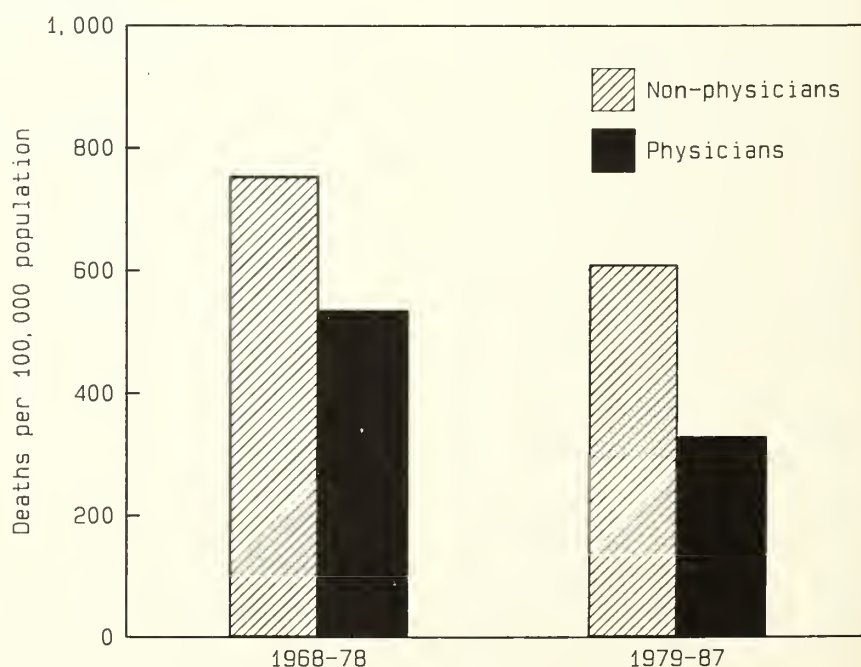
Location/ Occupation	Percentage who smoke cigarettes		
	1965	1975	1985
United States	51	42*	31
Rhode Island	NA	44	31
Physician**	33	19	9
Nonphysician	NA	44	31

NA = Not available.

* US Population surveyed in 1974.

**Rhode Island physicians surveyed in 1963, 1973, and 1983.

Figure 1: Age-adjusted death rate from all causes among resident white men aged 25-64 years, by physician/nonphysician, Rhode Island, 1968-1978 and 1979-1987.



two sources of data; counts of deaths included retirees, and population estimates did not.

From 1968 through 1987, 89,593 white males died in Rhode Island, including 420 physicians. Smoking-related cancers accounted for 11% of deaths, and heart disease and stroke for 50%. Among persons aged 25-64 years, mortality from all causes declined substantially — among physicians, 38%; among nonphysicians, 19% (Figure 1). Among physicians, smoking-related cancer mortality decreased 38%, compared with a 3% decline among nonphysicians (Figure 2). Mortality from heart disease and stroke declined 57% among physicians and 32% among nonphysicians (Figure 3).

These findings indicate that for the two periods compared (1968-1978 and 1979-1987), white male physicians in Rhode Island experienced greater declines in overall mortality, smoking-related cancers, and cardiovascular diseases than did white males in other occupations. However, these findings are based in part on relatively small numbers of deaths among small populations. Nevertheless, the results strongly suggest that at least half the current cardiovascular and smoking-related cancer mortality among white men aged 25-64 in Rhode Island may be preventable by reductions in smoking rates to the low levels currently observed among physicians.

[Excerpted with modifications from Scott, HD, *et al.* Smoking-related mortality decline among physicians — Rhode Island. *Morbidity and Mortality Weekly Review* 1990;39:656-8.]

Figure 2: Age-adjusted death rate from smoking-related cancers among resident white men aged 25-64 years, by physician/nonphysician, Rhode Island, 1968-1978 and 1979-1987.

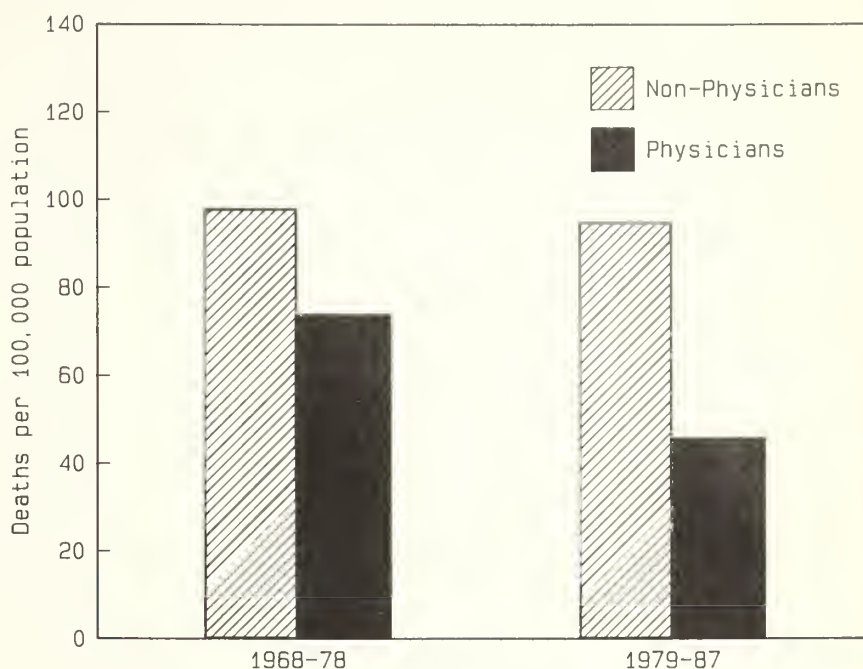
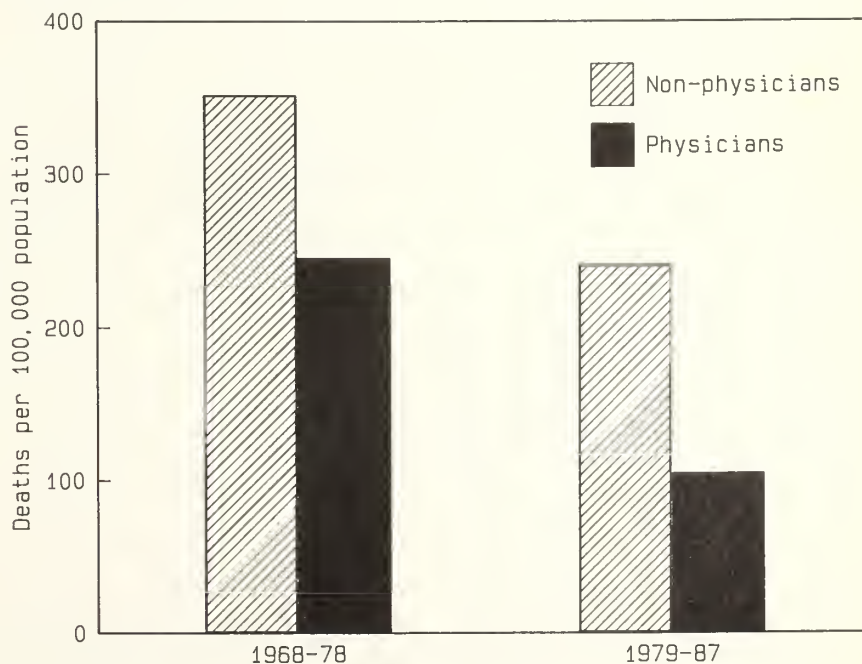


Figure 3: Age-adjusted death rate from heart disease and stroke among resident white men aged 25-64 years, by physician/nonphysician, Rhode Island, 1968-1978 and 1979-1987.



R H O D E
STATE OF ISLAND

Monthly Vital Statistics Report

Provisional Occurrence Data From the Division of Vital Records

H. Denman Scott, MD, MPH
Director of Health

Roberta A. Chevoia
State Registrar

Vital Events	Reporting Period	12 Months Ending with August 1990	
	August 1990 Number	Number	Rates
Live Births	1,497	15,768	15.8*
Deaths	733	9,795	9.8*
Infant deaths	(11)	(146)	9.3†
Neonatal deaths	(10)	(114)	7.2†
Marriages	797	8,192	8.2*
Divorces	309	3,884	3.9*
Induced Terminations	700	7,867	498.9†
Spontaneous Fetal Deaths	66	1,143	72.5†
Under 20 weeks' gestation	(61)	(1,044)	66.2†
20 + weeks' gestation	(5)	(91)	5.8†

*Rates per 1,000 estimated population.

†Rates per 1,000 live births.

Underlying Cause of Death Category	Reporting Period	12 Months Ending with May 1990		
	May 1990 Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	322	3,436	344.3	4,772.0
Malignant Neoplasms	196	2,419	242.4	6,726.5
Cerebrovascular Diseases	41	594	59.5	694.5
Injuries (Accident, Suicide, Homicide)	35	438	43.9	9,542.0
COPD	29	357	35.8	349.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 current estimated population of 998,000.

(c) Years of Potential Life Lost (YPLL)

NOTE: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME I
NUMBER 1

PROVIDENCE, R. I., JANUARY, 1917

PER YEAR \$2.00
SINGLE COPY, 25 CENTS

THE RHODE ISLAND MEDICAL JOURNAL HERITAGE

Fifty Years Ago (December, 1940)

The lead scientific article, written by Dr Paul Appleton, advocates the use of abdominal X-ray studies as an aid to the diagnosis of placenta previa. The author points out that while placenta previa may indeed be diagnosed by history, signs and confirmatory pelvic examination, such conventional procedures carry considerable risk. The pelvic examination, he reminds the reader, must be conducted under the most aseptic of circumstances since placenta previa is susceptible to infection as well as to induced hemorrhage, both of which can be furthered by such physical examination. Dr Russell Hunt, Roentgenologist to the Providence Lying-In Hospital has conducted soft tissue antero-posterior studies, both before and after the injection of an opaque medium into the bladder, and has thus been able to demonstrate clearly the location of the placenta in the gravid uterus. The cystogram, in the presence of placenta previa, may show, for example, an increase in the space between the fetal head and the bladder shadow. This X-ray procedure is strongly advocated.

The second paper reports on

thirteen years of experience in the use of an obstetrical bag at Providence Lying-In Hospital. The author, Dr Craig Houston, concludes: "As a result of this study, my opinion is that there is a place for the bag in obstetrics but it must be remembered that there is considerable risk to the mother and an extremely high foetal mortality. It does not seem advisable to attempt bagging unless the cervix is easily dilatable as failures were frequent with a rigid cervix. In the past few years simple rupture of the membranes has replaced use of the bag in cases of marginal placenta previa where the cervix is easily dilatable, while cases of central and partial placenta previa and cases with a rigid cervix are better treated by Caesarian section. I think that the use of a bag is seldom indicated to induce labor or to hasten dilatation of the cervix, as the danger of infection is great and failure of the bag to accomplish dilatation is very frequent."

A third obstetrical paper, by Dr Walter S. Jones, describes the Providence Lying-In Hospital Toxemia Clinic. This article is a preliminary report and serves to explain the basic problems of diagnostic classification. The toxemias of pregnancy are divided by the author into Group A (diseases not peculiar to pregnancy)

and Group B, the true toxemias which embrace both pre-eclampsia and eclampsia. In both Groups A and B, the more severe cases may be accompanied by convulsions. Amongst the disorders assigned to Group A are the following: hypertensive disease (benign or malignant), chronic vascular nephritis (end stage of malignant hypertension), glomerulonephritis (acute or chronic), nephrosis, and yet other forms of primary renal disease such as pyelonephritis. It is the aim of the clinic to maintain contact with their toxemia patients for many years particularly during subsequent pregnancies so as to provide some longitudinal experience in the clinical course of these various disorders.

The lead editorial discusses new revisions of the Federal Narcotic Regulations (1938) which has eliminated "... the provision requiring that the diagnosis or an alternate endorsement be indicated on prescriptions for narcotics for use in the treatment of incurable patients and for aged and infirm addicts; the physician is not now required to indicate the nature of the case in the execution of such prescriptions."

Minutes of the major Rhode Island Medical Society Committees are summarized in this issue. These include committees on: in-

dustrial health, cancer, child health, emergency relief, annual commercial exhibits, public health clinics, grievance and necrology.

The State Department of Health provides a written explanation of the 1938 state law requiring premarital physical examinations. The law states: "... no (marriage) license shall be issued ... until there shall be a statement ... signed by a licensed physician that each applicant has submitted to a physical examination and a Wasserman or Kahn ... test and that in the opinion of such physician the person is not infected with tuberculosis in the infectious stages nor with syphilis or gonorrhea." The article details many of the intricacies of this law.

Twenty Five Years Ago (December, 1965)

This issue of the *Journal* summarizes a symposium on the medical and surgical aspects of liver disease and is authored by Drs Robert V. Lewis, George F. Grady, Robert L. Scheig and Woodrow W. Lindenmuth. Lewis, in introducing the symposium, points out that it is only during the last two decades that "Anglo-American medicine" has acquired an increasing clinical and scientific understanding of liver disease. Many of these advances may be ascribed to the increasing use of liver biopsy and the improved knowledge of the biochemistry and physiology of hepatic metabolism. Grady discusses the failures thus far in trying to isolate the virus (or viruses) of hepatitis but he indicates evidence that the responsible agent(s) are transmitted by fecal contamination or, parenterally, through the mechanism of trans-

fusion or the use of contaminated needles or instruments. With regard to parenteral transmission, Grady also warns that high standards of blood donor selection must be maintained because relaxation of these blood bank standards "... frequently leads to extraordinarily high rates of serum hepatitis, particularly when narcotics addicts sell their blood." Scheig discusses the fatty acid profile and chemical composition of livers derived from rats fed ethanol or glucose and concludes that fatty infiltration of the liver is not a prelude to chronic liver disease such as Laennec's cirrhosis. Lindenmuth concludes the symposium with a discussion concerning surgical treatment of certain complications of hepatic cirrhosis, particularly the portacaval shunt. He recommends the following criteria for surgery: esophageal varices are bleeding; the patient is not near or in coma; the patient is a reasonable operative risk; an adequate blood supply is available; and, a well-rested and testing operating team is available.

Dr Milton Hamolsky provides a discussion of the thyroid gland in pregnancy, first a consideration of the alteration of thyroid function during normal pregnancy and then the role of both the normal and abnormal thyroid in disorders of menstruation, conception and pregnancy. He notes that the clinical manifestations of both hypothyroidism and hyperthyroidism in pregnancy are affected by the increased plasma binding capacity for thyroid hormone.

Dr Frank Cutts discusses the management of coronary artery disease and notes the importance of a low fat diet. He concludes, "... presently available medical treatment undoubtedly prolongs life and diminishes disability. However, fully effective control and prevention of this common

disease must await an understanding of the causes of the disturbed physiology and the development of living habits or drugs and hormones, that will prevent the development of the atherosclerosis in the coronary arteries."

Dr Jordan J. Cohen presents a brief synopsis of hydrogen ion metabolism showing simplified algebraic methods for an analysis of disturbances in hydrogen ion concentration and balance.

The lead editorial, written by Dr Alex Burgess, Sr, concerns the relative importance of morbidity and mortality in the later years of life. "In our judgment the decrease in *mortality* is of declining importance as an objective in this age group, because life expectancy is not greatly extended by the elimination of any one malady, whereas the *morbidity*, the terrible years of crippling before death brings relief, should be a prime objective of our professional endeavors."

The House of Delegates of the Rhode Island Medical Society, in a special meeting held on November 10, 1965, voted for the following actions: endorsing a mass immunization campaign in the state of Rhode Island against measles, to be sponsored by the Society; notifying the federal government that the Society's Physician Service be named as carrier to implement Part B of the federal act amending the Social Security Law; and, authorizing the Council to make inquiries and to take appropriate action respecting the availability of federal funds, under the new Medical Library Assistance Act, for the improvement of the Society's library.

4820 041



VASOTEC

(ENALAPRIL MALEATE) MSD

VASOTEC is available in 2.5-mg, 5-mg, 10-mg, and 20-mg tablet strengths.

Contraindications: VASOTEC* (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor.

Warnings: Angioedema. Angioedema of the face, extremities, lips, tongue, glottis, and/or larynx has been reported in patients treated with ACE inhibitors, including VASOTEC. In such cases, VASOTEC should be promptly discontinued and the patient carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL), should be promptly administered.** (See ADVERSE REACTIONS.)

Hypotension: Excessive hypotension is rare in uncomplicated hypertensive patients treated with VASOTEC alone. Patients with heart failure given VASOTEC commonly have some reduction in blood pressure, especially with the first dose, but discontinuation of therapy for continuing symptomatic hypotension usually is not necessary when dosing instructions are followed, caution should be observed when initiating therapy. (See DOSAGE AND ADMINISTRATION.) Patients at risk for excessive hypotension, sometimes associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death, include those with the following conditions or characteristics: heart failure, hypotension, high-dose diuretic therapy, recent intensive diuresis or increase in diuretic dose, renal dialysis, or severe volume and/or salt depletion of any etiology. It may be advisable to eliminate the diuretic (except in patients with heart failure), reduce the diuretic dose, or increase salt intake cautiously before initiating therapy with VASOTEC in patients at risk for excessive hypotension who are able to tolerate such adjustments. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients at risk for excessive hypotension, therapy should be started under very close medical supervision and such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart disease or cardiovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of VASOTEC, which usually can be given without difficulty once the blood pressure has stabilized. If symptomatic hypotension develops, a dose reduction or discontinuation of VASOTEC or concomitant diuretic may be necessary.

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause granulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: General Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including VASOTEC, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or VASOTEC may be required.

Evaluation of patients with hypertension or heart failure should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalemia was observed in 3.8% of patients, but was not a cause for discontinuation.

Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with VASOTEC. (See Drug Interactions.)

Surge/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta-adrenergic blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine, prazosin, and digoxin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC attenuates potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure receiving VASOTEC.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant VASOTEC and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

Radioactivity was found to cross the placenta following administration of labeled enalapril to pregnant hamsters. There are no adequate and well-controlled studies of enalapril in pregnant women. However, data are available that show enalapril crosses the human placenta. Because the risk of fetal toxicity with the use of ACE inhibitors has not

been clearly defined, VASOTEC* (Enalapril Maleate, MSD) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome: Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypotension, or the underlying prematurity.

Nursing Mothers: Milk in lactating rats contains radioactivity following administration of ¹⁴C enalapril maleate. It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2967 patients.

HYPERTENSION: The most frequent clinical adverse experiences in controlled trials were: headache (5.2%), dizziness (4.3%), and fatigue (3%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.4%), nausea (1.4%), rash (1.4%), cough (1.3%), orthostatic effects (1.2%), and asthenia (1.1%).

HEART FAILURE: The most frequent clinical adverse experiences in both controlled and uncontrolled trials were: dizziness (7.9%), hypotension (6.7%), orthostatic effects (2.2%), syncope (2.2%), cough (2.2%), chest pain (2.1%), and diarrhea (2.1%).

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in both controlled and uncontrolled clinical trials were: fatigue (1.8%), headache (1.8%), abdominal pain (1.6%), asthenia (1.6%), orthostatic hypotension (1.6%), vertigo (1.6%), angina pectoris (1.5%), nausea (1.3%), vomiting (1.3%), bronchitis (1.3%), dyspnea (1.3%), urinary tract infection (1.3%), rash (1.3%), and myocardial infarction (1.2%).

Other serious clinical adverse experiences occurring since the drug was marketed or adverse experiences occurring in 0.5% to 1% of patients with hypertension or heart failure in clinical trials in order of decreasing severity within each category:

Cardiovascular: Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high-risk patients (see WARNINGS, Hypotension), pulmonary embolism and infarction, pulmonary edema, rhythm disturbances, atrial fibrillation, palpitation.

Digestive: Ileus, pancreatitis, hepatitis (hepatocellular or cholestatic jaundice), melena, anorexia, dyspepsia, constipation, glossitis, stomatitis, dry mouth.

Musculoskeletal: Muscle cramps.

Nervous/Psychiatric: Depression, confusion, ataxia, somnolence, insomnia, nervousness, paresthesia.

Urogenital: Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

Respiratory: Bronchospasm, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection.

Skin: Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pruritus, alopecia, flushing, hyperhidrosis.

Special Senses: Blurred vision, taste alteration, anosmia, tinnitus, conjunctivitis, dry eyes, tearing.

A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgias, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash, and other dermatologic manifestations.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients following the initial dose or during extended therapy. Hypotension or syncope was a cause for discontinuation of therapy in 1.8% of hypertensive patients. In heart failure patients, hypotension occurred in 6.7% and syncope occurred in 2.2% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 1.9% of patients with heart failure. (See WARNINGS.)

Clinical Laboratory Test Findings

Serum Electrolytes: Hyperkalemia (see PRECAUTIONS), hyponatremia.

Creatinine, Blood Urea Nitrogen: In controlled clinical trials, minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.) In patients with heart failure who were also receiving diuretics with or without digitalis, increases in blood urea nitrogen or serum creatinine, usually reversible upon discontinuation of VASOTEC and/or other concomitant diuretic therapy, were observed in about 11% of patients. Increases in blood urea nitrogen or creatinine were a cause for discontinuation in 1.2% of patients.

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in either hypertension or heart failure patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): In marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported. A few cases of hemolysis have been reported in patients with G6PD deficiency.

Liver Function Tests: Elevations of liver enzymes and/or serum bilirubin have occurred.

Dosage and Administration: Hypertension: In patients who are currently being treated with a diuretic, symptomatic hypotension occasionally may occur following the initial dose of VASOTEC. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with VASOTEC to reduce the likelihood of hypotension. (See WARNINGS.) If the patient's blood pressure is not controlled with VASOTEC alone, diuretic therapy may be resumed.

If the diuretic cannot be discontinued, an initial dose of 2.5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.)

The recommended initial dose in patients not on diuretics is 5 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 10 to 40 mg per day administered in a single dose or in two divided doses. In some patients treated once daily, the antihypertensive effect may diminish toward the end of the dosing interval. In such patients, an increase in dosage or twice-daily administration should be considered. If blood pressure is not controlled with VASOTEC alone, a diuretic may be added.

Concomitant administration of VASOTEC with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium. (See PRECAUTIONS.)

Dosage Adjustment in Hypertensive Patients with Renal Impairment: The usual dose of enalapril is recommended for patients with a creatinine clearance > 30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 2.5 mg once daily. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Heart Failure: VASOTEC is indicated as adjunctive therapy with diuretics and digitalis. The recommended starting dose is 2.5 mg once or twice daily. After the initial dose of VASOTEC, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) If possible, the dose of the diuretic should be reduced, which may diminish the likelihood of hypotension. The appearance of hypotension after the initial dose of VASOTEC does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension. The usual therapeutic dosing range for the treatment of heart failure is 5 to 20 mg daily given in two divided doses. The maximum daily dose is 40 mg. Once-daily dosing has been effective in a controlled study, but nearly all patients in this study were given 40 mg, the maximum recommended daily dose, and there has been much more experience with twice-daily dosing. In addition, in a placebo-controlled study which demonstrated reduced mortality in patients with severe heart failure (NYHA Class IV), patients were treated with 2.5 to 40 mg per day of VASOTEC, almost always administered in two divided doses. (See CLINICAL PHARMACOLOGY, Pharmacodynamics and Clinical Effects.) Dosage may be adjusted depending upon clinical or hemodynamic response. (See WARNINGS.)

Dosage Adjustment in Patients with Heart Failure and Renal Impairment or Hyponatremia: In patients with heart failure who have hyponatremia (serum sodium < 130 mEq/L) or with serum creatinine > 1.6 mg/dL, therapy should be initiated at 2.5 mg daily under close medical supervision. (See DOSAGE AND ADMINISTRATION, Heart Failure, WARNINGS, and PRECAUTIONS, Drug Interactions.) The dose may be increased to 2.5 mg b.i.d., then 5 mg b.i.d. and higher as needed, usually at intervals of four days or more, if at the time of dosage adjustment there is not excessive hypotension or significant deterioration of renal function. The maximum daily dose is 40 mg.

For more detailed information, consult your MSD Representative or see Prescribing Information, Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19380 J9V561R2(8/20)

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VASOTEC is generally well tolerated and not characterized by certain undesirable effects associated with selected agents in other antihypertensive classes.

VASOTEC is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor. A diminished antihypertensive effect toward the end of the dosing interval can occur in some patients.

For a Brief Summary of Prescribing Information, please see the last page of this advertisement.

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